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# ENDEAVOUR

Volume XI Number 42

APRIL 1952

*The drawing on the cover is of the bark* Endeavour, *which, commanded by Captain James Cook and carrying a number of scientific workers, was sent out by the British Admiralty in* 1768 *to chart the South Pacific Ocean and observe the transit of Venus*

# ENDEAVOUR

A quarterly review designed to record the progress of the sciences in the service of mankind

VOLUME XI April 1952 NUMBER 42

# CONTENTS




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# Leonardo da Vinci as scientist

Leonardo da Vinci was born 500 years ago this month, so that the present occasion is a fitting opportunity to pay tribute to one who might well dispute with Aristotle the distinction of having been '*maestro di color che sanno*.' Fired with enthusiasm for his illustrious countryman, one of our Italian readers, Professor Siro Taviani (himself a native of Vinci), has sent us an astonishing catalogue of Leonardo's contributions to *quattrocento* and *cinquecento* science, and we gladly make use of some of the material with which Professor Taviani's erudition has furnished us.

What gives Leonardo his outstanding position in the history of human achievement is his combination of artistic genius with exceptional scientific insight, and a fertility of ideas which not only led him to recognize problems unperceived by others, but often to solve a problem as soon as it was posed. His intellectual interests ranged far and wide, and whatever he studied he illumined. His powers of observation have probably never been excelled, if equalled; he had, for example, the faculty of seeing successive changes in a moving object much as they are shown in a slow-motion film, and perhaps this peculiarity of vision was in some way connected with his specular, or mirror-image, handwriting.

Leonardo's outlook on science was rationalistic. He considered the experience of the senses as the foundation of all knowledge, but added that such experience must afterwards be elaborated by the intellect: observational and experimental results open the road for rational study to follow. He appreciated the importance of the quantitative as against the contemporary qualitative approach, and he accepted the principle of causality in the sense in which it has been generally adopted by succeeding men of science. The spirit of science showed itself again in his reluctance to draw general conclusions from inadequate data.

In the field of astronomy, Leonardo has been credited with anticipation of the Copernican theory, largely on the strength of a jotting of his preserved in the Royal Library at Windsor: 'the Sun stands still.' This evidence is too slight to carry conviction, but there is no doubt that he had some intuition of several astronomical facts ascertained only centuries later. He was able to calculate the dimensions of the Earth, and he made penetrating speculations on the size of stars, on the light and heat of the Sun, on the luminosity of the planets and the Moon, and on the relation between the Moon and the Earth, often reaching correct conclusions.

More important was his work on pure and applied mechanics, which was always his favourite study and to which he made noteworthy original contributions. He went far beyond the general knowledge of his time in his treatment of the theory of levers, and of the conditions for equilibrium on an inclined plane, and he was able to solve numerically the problem of the composition and resolution of forces. Systems of fixed and moving pulleys interested him, and led him to a comprehension of the principle of virtual work. He gave an almost exact enunciation of the law of inertia, had a clear idea of the principle of action and reaction, recognized that the velocity of a freely falling body increases linearly with time, and knew the absurdity of trying to contrive perpetual motion.

Leonardo made a series of fundamental discoveries in hydrostatics. Thus he discovered the equality of liquid pressure in all directions 150 years before it was rediscovered by Pascal; he outlined the laws of liquid pressure in communicating vessels, and was well aware of the so-called hydrostatic paradox attributed to Stevinus (1548–1620). He had some knowledge also of the small compressibility of water, of the phenomena of capillarity, and of the properties of siphons.

Other branches of physics captured Leonardo's restless imagination, particularly optics. He investigated the structure of the eye, explained the role of the crystalline lens and the iris, recognized the importance of the optic axis, and understood the principle of stereoscopic vision. He attributed the formation of images on the retina to the same principle as that which operates in a *camera obscura*, of which he was the first to give a perfectly clear description. Leonardo also studied the reflection of light at plane and spherical surfaces, and planned the construction of parabolic concave mirrors. He was interested in lenses and their application to the correction of near and far sight, and it may be significant that in his notes he mentions spectacles by which 'to see the Moon very large.'

For the present age, some of Leonardo's most interesting investigations are those concerned with problems of flight. The subject was one which

fascinated him, and he clearly foresaw the possibility of constructing machines which should fly. He realized the complexity and diversity of the difficulties to be overcome, but had a firm belief that they would finally be surmounted. In his codex on the flight of birds, and in other notes, he describes several anemometers which he had invented; the disposition, elasticity, and resistance of wing feathers; and the motion of the wings in various phases of flight. He gave consideration to the problem of the lifting force, to the part played by the centre of gravity in the flight of birds and machines, and to the conditions of gliding both with and against the wind. Among his drawings is a complete plan for the construction of a glider; there is also a plan for a helicopter. He knew how a propeller should be employed for the propulsion of a flying machine, and in his *Codex Atlanticus* he gives the first known drawing of a parachute.

Leonardo's interest in physics did not confine itself to the pure science; he was equally interested in its applications in the fields of civil and military engineering, always proceeding from theoretical concepts to their practical realization. His ideas and inventions are too numerous to list, but they range from slum clearance and town planning to slewing-cranes, escalators, mechanical looms, pumps, floating dredgers, wire-drawing machines, transmission chains, pontoon bridges, and devices for lifting heavy guns.

After what has already been said, it might appear incredible that Leonardo should have found time for yet other excursions into the realm of knowledge, but in point of fact he carried out extensive work on the biological sciences, particularly anatomy. His beautiful anatomical drawings show the care with which he must have studied the human skeleton, the joints and muscles, the brain, nerves, and spinal chord, the heart and the blood vessels, and the urinogenital system. The assemblage of muscles regulating the right ventricle of the heart is still called after him. As an artist, he would have been especially interested in facial expressions, and he drew and described the muscles which control them. He was also interested in voice production, and understood the function of the changes in shape of the oral cavity in the pronunciation of vowels and that of the lips and tongue in the pronunciation of consonants.

This account, necessarily very incomplete, of Leonardo's scientific work, would in itself suffice to show his profound intelligence and his prodigious activity; but when we remember that he was also one of the greatest of all artists we are left with a deep feeling of wonderment 'that one small head could carry all he knew.'

Leonardo's voluminous writings and drawings are widely scattered among the principal libraries of the world, and it is therefore pleasant to know that, under the auspices of the Italian Government, reproductions of them are being collected into a comprehensive *Corpus Vincianum*.

# In memoriam: Allan Ferguson (1880–1951)

It is with deep regret that we record the death of Dr Allan Ferguson, which occurred shortly after our January 1952 issue went to press. Ferguson was one of the original members of the editorial advisory panel of ENDEAVOUR and gave unstinted help and advice. As one of the referees on physical subjects he was often trenchant in his criticism but invariably kindly, and he was fruitful in suggesting topics for physical and other articles. A man of wide scholarship—his private library of some 12,000 volumes bore witness to the catholicity of his learning—he was particularly interested in the literary style of ENDEAVOUR and was quick to point out any slovenliness or obscurity of writing. He was beloved by all the staff and advisory panel, and his death comes as a severe blow.

Ferguson was born at Entwistle, near Bolton, England, on 11th May, 1880, and was educated at the Harris Institute, Preston, and University College, Bangor, where he subsequently became assistant lecturer in physics. He later became lecturer in physics at the Manchester College of Technology and assistant professor of physics in the University of London (Queen Mary College). He was editor of *The Philosophical Magazine*, and from 1936 to 1946 general secretary of the British Association for the Advancement of Science. He was secretary (1928–38) and then president (1938–41) of the Physical Society, and acted as advisory editor to various scientific publications, where his acute critical faculty was invaluable. He died peacefully on 9th November, 1951, at Bishop's Stortford, Hertfordshire.

# Pile-produced radioactive materials and their uses

W. J. ARROL

The preparation and distribution of radioactive materials from the larger of two piles is the principal task of the isotopes division at Harwell, and the Ministry of Supply's radiochemical centre at Amersham, England. From Harwell alone, more than eight hundred shipments a month are made, the recipients being industrial and academic scientists, and, in particular, medical and biochemical research workers. An elaborate organization exists to satisfy these widely varying needs, and to make sure that the pile is used in the most efficient way possible.

For the purposes of this article, the Harwell pile, which consists of a lattice of uranium and graphite, may be regarded simply as a large neutron source enclosed in a concrete shield, into which materials may be inserted for irradiation, and from which they may be withdrawn radioactive. The north face of the Harwell pile is shown in figure 5. Isotopes are removed through a bridge containing a lead-lined channel. The aluminium containers in which the irradiation is effected can be seen in transference through a flexible tube to a heavy lead safe, ready to be wheeled away.

The nucleus of every atom carries a positive charge equal to the atomic number, and is surrounded by as many negatively charged electrons. When changes in the nucleus are to be brought about by bombarding it with charged particles such as protons, deuterons, and $\alpha$-particles, these must be moving with high energy if they are to penetrate the electron cloud and overcome the electrostatic repulsion between the target nucleus and themselves. Neutrons, however, are uncharged, and can pass easily into a nucleus even though they are moving slowly. They are therefore particularly useful for inducing nuclear reactions.

The commonest nuclear reaction brought about by neutrons is that in which a neutron is absorbed in a target nucleus and a $\gamma$-ray emitted. This is called an $(n,\gamma)$ reaction. Such a reaction can be written in a concise form; the formation of sodium 24 from sodium 23, for example, is written $Na^{23}(n,\gamma)Na^{24}$. No change in the charge on the nucleus occurs, and the product nucleus is therefore chemically the same as the target. A practical example is the preparation of radioactive sodium chloride, in which the sodium is partially converted to sodium 24, of 15-hour half-life. Ordinary sodium chloride is irradiated in the pile at a high neutron flux for several days. It emerges brown in colour, this colour disappearing if the material is heated or dissolved in water. In addition to the $Na^{24}$ activity produced, a short-lived activity is induced in the chlorine owing to the reaction $Cl^{37}(n,\gamma)Cl^{38}$, and negligibly small amounts of other activities are also present. When the $Cl^{38}$ has decayed, therefore, we have a sample of salt the same chemically as it was before, but with its sodium 'labelled' with $Na^{24}$. It can be dissolved in water to form a solution isotonic with blood, sterilized, and used for such medical purposes as the determination of total body sodium [1].

When the $\gamma$-ray is emitted in the $(n,\gamma)$ process, the newly formed atom recoils in the opposite direction with enough energy to tear it out of the chemical combination in which it was held in the target compound. The chemical form in which it ends may be quite different. In the case of an ionic lattice like sodium chloride, the $Na^{24}$ moves in the lattice but remains an ion, and when the irradiated salt is dissolved in water it is indistinguishable from ordinary $Na^{23}$ ions. The preparation of a compound labelled in the desired manner simply by irradiating the identical compound in the pile is, however, the exception rather than the rule. The best practice is to irradiate elements or their simplest possible compounds, and then to convert the active substance into the desired chemical form afterwards.

Several nuclear reactions can be induced with neutrons in which the neutron is absorbed in the nucleus of the target atom and a charged particle is emitted instead of a $\gamma$-ray. Such reactions are known as (n,p) and $(n,\alpha)$ reactions, when a proton and an $\alpha$-particle respectively are emitted. In these cases, the charge on the nucleus is changed, so that the product nucleus differs chemically from the target nucleus, and the radioactive

material should theoretically be separable without any inactive isotope being present. In practice, it is usually not possible to prepare such truly carrier-free material, and the use of this term should be treated with some reserve. However, it does imply that the material is of very high specific activity.

Other nuclear processes used to prepare carrier-free materials are (i) the (n,γ) processes, in which the original product is radioactive and undergoes β-decay to the desired radioactive atom, and (ii) the fission process. The fission of uranium 235 produces many radioactive species, all of which are chemically different from uranium. They can be prepared at very high specific activity. A third method of preparing material of high specific activity—which is, however, not carrier-free—is the Szilard-Chalmers process; this makes use of the recoil of a newly formed atom from the γ-ray of the (n,γ) process [2]. If, for example, iron is irradiated in the form of potassium ferrocyanide, atoms of iron undergoing recoil will be torn from the ferrocyanide ions, and a good proportion of them will appear as ferric iron, which may be separated from the rest of the target ferrocyanide and obtained at a specific activity nearly a thousand times as great as that induced by the irradiation of elementary iron [3].

## RADIATION AND HEALTH PRECAUTIONS

Radioactive substances decay by several different processes, but the commonest mode of decay of those produced in the pile is by the emission of β-particles (high-energy electrons). The β-particles are very often accompanied by γ-rays, which are of the same nature as X-rays but usually more energetic. α-particles, which are positively charged helium nuclei, are usually emitted only by heavy elements.

The unit of radioactivity is the curie, which is defined as that amount of radioactive material undergoing $3{\cdot}7 \times 10^{10}$ disintegrations per second. This is approximately the disintegration rate of a gram of radium, and represents an amount of radioactive material which must be treated with great respect.

Shielding is usually necessary against the radiations from radioactive materials; this is because of their effects on living matter in general and on the human body in particular. The deleterious effects of ionizing radiations on the body are well understood, through the experience gained during the early days of X-ray and radium therapy. It has been possible to ascertain maximum doses of radiation which may be taken by workers with radioactive substances throughout their working lives without serious chance of radiation damage of any kind. These are known as tolerance doses. The shielding and other precautions necessary to cut radiation dose-rates to less than tolerance levels depend on the nature of the source and of the radiations from it [4].

α-particles have a short range in matter. They are stopped by a few centimetres of air at normal pressure, and their tracks are straight. Protection is usually obtained by working inside a Perspex dry-box (figure 3), manipulations being carried out with the hands protected by rubber gloves, through which the α-particles cannot pass. The greatest danger from α-active materials arises from possible ingestion into the body through the breathing of active dust, and intensive precautions against dust are necessary. Few α-active materials are used for medical or industrial purposes.

The ranges of β-particles in air vary enormously with their energies. The least energetic are absorbed in a few millimetres of air at normal pressure, while the most energetic may have a path-length of several metres. Unlike α-particles, they are readily scattered, and an individual β-particle will move in many different directions before being finally stopped. Even energetic β-rays are stopped by about a centimetre of Perspex or plate glass, and very active sources may be manipulated behind screens of these materials.

γ-radiation is absorbed exponentially in matter, and sources of the order of curies must be shielded with up to about ten centimetres of lead to reduce the radiation to a tolerable level, the thickness depending on the energy of the radiation. Manipulation of γ-sources behind such thick walls is naturally rather awkward.

## MEASUREMENT OF RADIOACTIVITY

Many of the uses of radioactive materials depend on the extreme sensitivity with which they can be measured. The atoms of one curie of truly carrier-free phosphorus 32, for example, together weigh about $4 \times 10^{-6}$ g, and, as it is quite easy to measure as little as $3 \times 10^{-10}$ curies of this material, the actual mass of phosphorus 32 which may be measured is of the order of $10^{-15}$ g. It is also necessary to have means of measuring high activities of the order of curies, particularly in the case of γ-sources prepared in the pile. For this purpose, very insensitive measuring devices are sufficient.

Most measurement devices are based on one of

three effects which radiations can produce. These are:

1. Ionization of gases.
2. Scintillation effects.
3. Photographic effects.

(1) In its passage through a gas, an α-, β-, or γ-ray interacts with molecules in such a way that an electron is torn away from the molecule. The electron, which is negatively charged, and the residue of the molecule, which is now positively charged, constitute an ion pair. If during the ionization process the gas is subjected to an electric field of appropriate strength, the electrons will move to the positive pole and the positive ions to the negative pole, so that an electric current passes through the gas. This current is proportional to the number of ionizing radiations per second passing through a given volume of gas, and therefore proportional to the source strength.

Ionization current measurement is used directly in the ionization chamber (figure 4), which is of general use for measurements of γ-radiation, and chambers can be constructed to cover a wide range of sensitivities. To a limited extent they can be used for β-ray detection as well [5].

Many of the early measurements of radioactive sources were made with gold-leaf electroscopes. If the air in a charged gold-leaf electroscope is rendered conducting by ionizing radiations from a radioactive source, then the rate of discharge between two predetermined positions of the leaf can be arranged to be proportional to the source strength. The early gold-leaf electroscope was quite accurate but very insensitive. In its more modern form, such as the Lauritsen electroscope, where the gold leaf is replaced by a gold-plated thin quartz fibre, the instrument can be both a sensitive and an accurate measuring device [6].

The most popular and versatile instrument for measuring small amounts of activity is the Geiger-Müller (or just Geiger) counter. In this case, the ionization of a gas by an individual β-particle, or by a secondary electron from a γ-ray, is used to trigger a discharge in the counter, the magnitude of the discharge being sufficient to enable it to operate electronic equipment and finally to be counted and registered mechanically. The Geiger counter consists essentially of a cylindrical conducting cathode, down the axis of which is stretched a thin, insulated tungsten wire charged positively with respect to the cathode at about 1000 volts. The counter is filled with a suitable gas; one of the fillings which has been most used is argon at a pressure of about 10 cm of mercury, with the addition of about 10 per cent. of alcohol vapour. With the correct conditions of gas filling and applied voltage, a discharge can be started by the appearance of a single ion pair inside the cathode.

The magnitude of the Geiger discharge is independent of the number of ion pairs in the track of the radiation which initiates it. The energy of the pulse is drawn from the high-voltage supply to the anode. When the discharge has reached its maximum, it must be stopped as soon as possible and the counter restored to its previous condition, in order to be ready for the next β- or γ-ray reaching it. This is done either by an external electronic quenching circuit or internally by the use of a quenching vapour. With the filling mixture given above, the alcohol functions in this manner. It is modern practice to use a quenching agent where possible, but to use a quenching circuit in addition, in order that the length of the insensitive time may be well defined and certain spurious discharges suppressed.

The counter is arranged in an envelope, usually with a thin window so that β-particles can pass inside. A popular type of bell jar counter is shown in figure 1(*a*). Counters for γ-rays do not need windows; a typical design is shown in figure 1(*c*). Energetic β-rays from radioactive solutions can be counted in a liquid counter, such as that designed by Veall (figure 1(*b*)) [7].

Geiger counters count practically all the β-particles which enter the space between cathode and anode. The overall efficiency for counting the β-rays from a source depends on the geometrical arrangement of source and counter, and on any absorptive material between the source and the active volume of the counter. The efficiency may be increased by scattering into the counter β-particles which would otherwise escape. γ-rays are counted by the secondary electrons which they knock out of the material close to the inside surface of the counter. Only about 1 per cent. of the γ-rays passing through the counter are counted, so that this is a relatively inefficient means of measuring γ-radiation.

Generally, only relative measurements of radioactive sources are needed, but there are special cases in which absolute activities must be measured. The Geiger counter in special forms and arrangements [8, 9] has been most useful in the absolute standardization of sources.

(2) Scintillations produced in fluorescent material under the impact of α-rays were observed in an instrument known as the spinthariscope. This was

one of the oldest methods of observing and counting the radiations from radioactive material. The tiny flashes could be observed by eye in a darkened room and counted by the observer. The scintillation method fell into disuse in the 1920's with the development of methods of measurement based on the ionization of gases, but it has been revived in the last few years as a highly efficient method of measuring all types of radiation, particularly γ-rays [10]. As phosphors, such materials as naphthalene, anthracene, and thallium-activated sodium and potassium iodides can be used, in the form of large single crystals several centimetres thick. A high proportion of incident γ-radiation is absorbed in a crystal of this size, and each γ-ray produces a minute flash of light which can affect the photocathode of an electron multiplier tube [5]. The pulse emerging from the electron multiplier is sufficiently large to actuate electronic counting equipment. Another advantage of the scintillation counter is that its complete and very rapid response to a γ-ray occupies much less than a microsecond, or considerably less than a hundredth of the time factor usually associated with a Geiger counter. Very high counting rates can therefore be used.

(3) Photographic methods of detecting radiations have been greatly developed in recent years. At the present time the principal use of the photographic method is in the detection of highly localized radioactive material. In the autoradiographic technique (often called the radioautographic technique in America) a flat specimen is placed in contact with a photographic emulsion. β-active material in the specimen affects the emulsion locally, and the developed plate can be compared with the specimen in order to see where the radioactivity is located. Among the many variants of the technique, that which produces the highest resolution is due to Pelc [11], who used a stripping emulsion floated in water on to the specimen and dried *in situ* for exposure. This can then be developed and fixed in contact with the specimen, and gives an immediate picture of the distribution of radioactivity. The resolution of autoradiographs prepared in this way is very high. Stevens [12] showed that lines of radioactive silver iodide 2–2·5 microns apart were fully separated in the autoradiograph. The order of magnitude of exposure necessary for the production of an autoradiograph is $(2–5) \times 10^6$ β-tracks per square centimetre of emulsion.

Photographic methods are suitable for the measurement of low levels of irradiation occurring over long periods. Workers with radioactive materials carry badges of X-ray film, which are developed weekly and provide a record of the β- and γ-radiation to which they have been exposed.

### ORGANIZATION OF SUPPLIES OF RADIOACTIVE MATERIALS

About half the shipments from Harwell consist of radioactive materials which do not need to be manipulated chemically before despatch. These are transferred to boxes having the appropriate shielding, are monitored to ensure that the radiation levels outside the boxes are satisfactorily small, and are then sent off. Materials which need chemical processing are safely boxed, and sent to the appropriate chemical laboratory. In all cases, no time is lost in getting the material to its destination. Short-lived radio-isotopes must obviously not be delayed. The shortest-lived material so far sent out regularly from Harwell is silicon 31, of half-life 170 minutes. This is sent by car to a university twenty miles away. Although it is less urgent for long-lived isotopes to reach their destinations quickly, it is convenient to use the best transport facilities.

One means of transporting active materials to South Africa is of particular interest. Protection from γ-radiation can be got by making use of the inverse square law. The wing-tips of South African Airways airliners are fitted with a compartment into which the source, in a light brass container, can be transferred at the airfield. The passengers and crew and the freight compartment are so far away from the wing-tip that the radiation level is far below tolerance when a source of many hundreds of millicuries is in the wing-tip container. This device was developed by the South African Department of Scientific and Industrial Research [13].

It is inevitable that an organization for handling orders for radioactive materials should develop its own technical parlance. Fortunately, most of the terms are self-explanatory. Incoming order-forms are divided into two main classes, namely those for material which has been chemically processed, and those requesting the irradiation of a definite amount of a substance under definite conditions for a definite time. The latter type of order is usually for what is called the irradiation unit of a material. The week's orders for irradiation units, together with any special requests, are numbered and compiled into the weekly 'canning list,' which is passed to the technical group of the isotopes division. Members of the technical group weigh

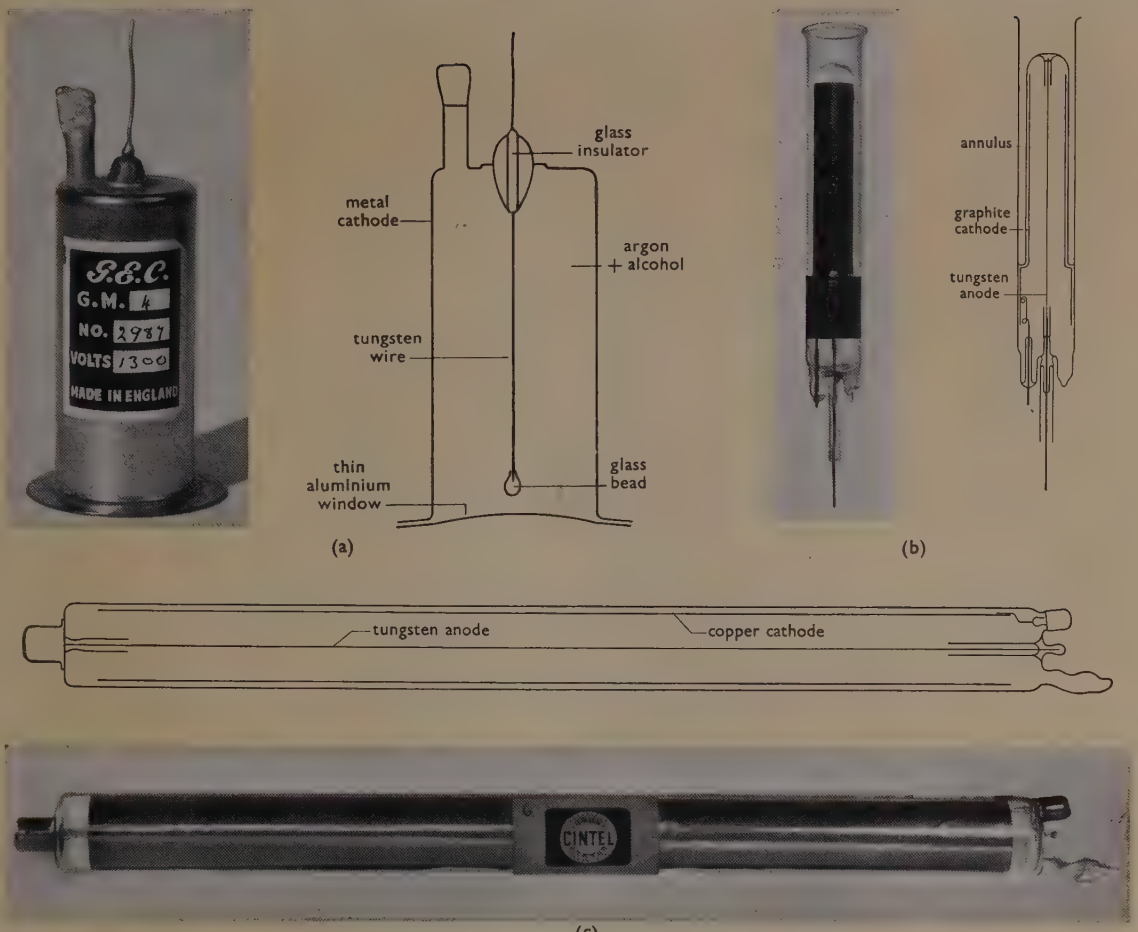


FIGURE 1 – *Instruments for the measurement of radiation.* (a) *End-window counter;* (b) *liquid counter;* (c) *γ-counter.*

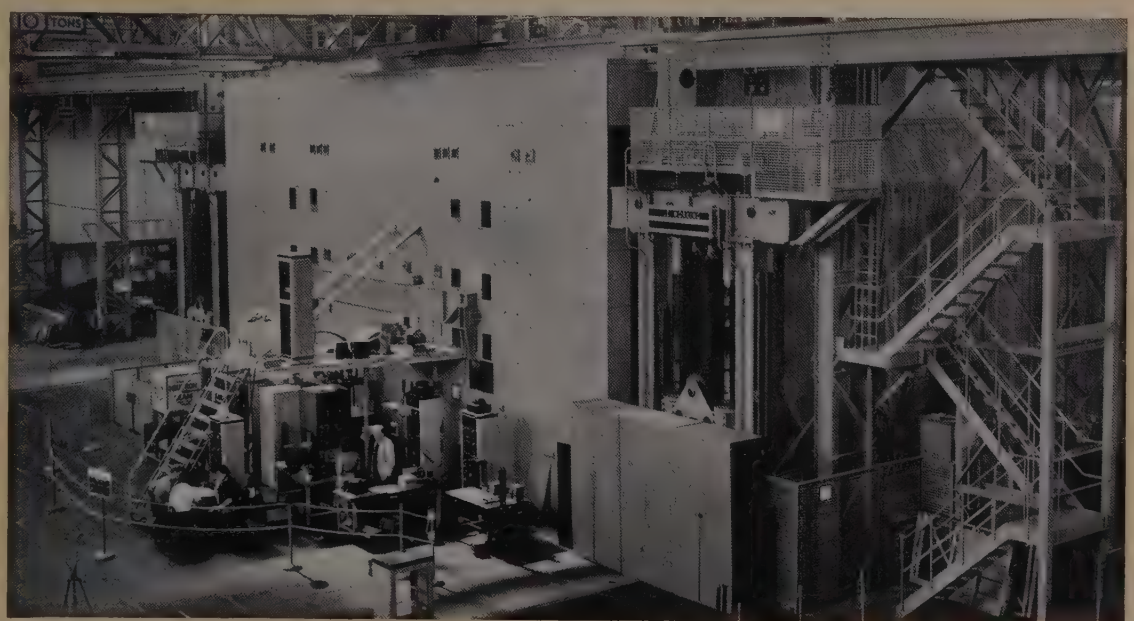

FIGURE 2 – *Experimental face of the large Harwell pile, showing lift and stairs to upper part. Beneath the equipment on the left is a laboratory with access to the pile below ground level.*

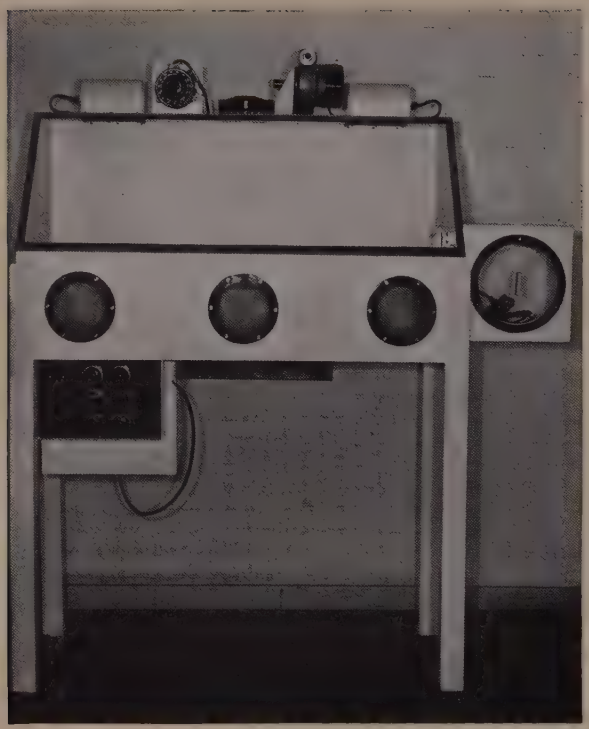

FIGURE 3 – *Perspex dry-box for the manipulation of radioactive material emitting α-particles.*

FIGURE 4 – *Pistol-grip monitor for measuring local intensity of radiation.*

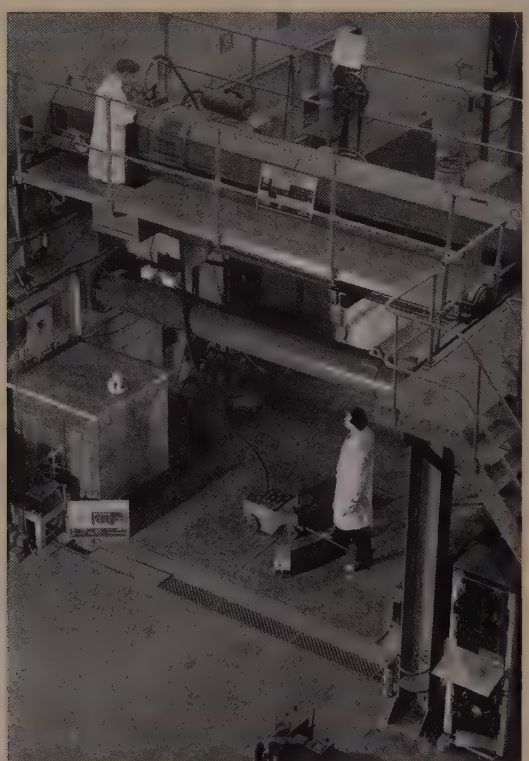

FIGURE 5 – *Control-face of the pile, showing the bridge by which isotopes are removed through a lead-screened channel. The aluminium containers in which the irradiation is effected are being transferred through a flexible tube to a heavy lead safe, ready to be wheeled away.*

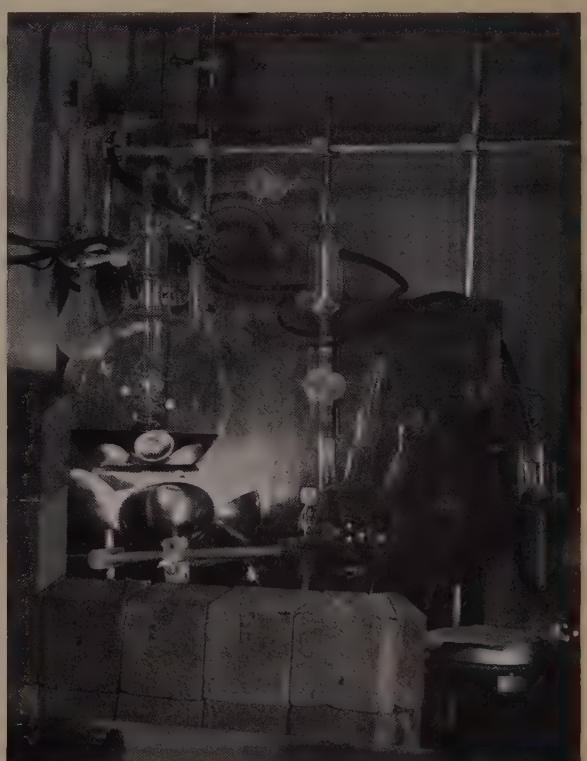

FIGURE 6 – *Apparatus for the preparation of iodine* 131. *Part of the heavy lead shield has been removed to give a clear view. Heating is by infra-red radiation.*

out the necessary pure chemicals into numbered aluminium cans. Each weighing, and particularly the identity of each chemical, are observed by two operators independently, in order to avoid mistakes. Other members construct a pile-loading diagram, showing the position that each can must occupy in the pile in order to induce the correct activity in its contents. The exponential build-up of activity in a sample can be calculated in terms of the nuclear properties of the sample and the irradiation conditions of the pile. Rapid calculations are made possible by the use of a circular slide rule designed by W. S. Eastwood [14].

Some elements absorb neutrons exceptionally readily, and samples of them can depress the neutron flux locally and so interfere with the irradiation of neighbouring samples. Similarly, such elements may interfere with their own irradiation, through the phenomenon of self-shielding. This occurs when enough neutrons are absorbed in the outer layers of the sample to reduce the activity induced in the inside, and the total activity produced in the sample may then be very much less than the calculated value. These effects can be minimized by careful consideration of the size of the highly absorbing samples, and of their distribution in the pile.

Materials to be irradiated in the pile must be scrutinized to make sure that they are chemically and physically suitable. The element to be irradiated must not be in a compound with other elements which absorb neutrons heavily, or which produce high unwanted activities. Solids must not melt, and liquids must not boil, under conditions somewhat more rigorous than pile conditions, and those materials which are likely to decompose are particularly suspect. Liquids of boiling-points at least 50–100° C higher than the pile temperature may be irradiated if they are chemically stable, and can be enclosed in fused silica ampoules. Fused silica is used for ampoules for the same reason as aluminium for cans: both absorb relatively few neutrons, and the activity induced in each is short-lived. Since this system of arranging and scrutinizing pile irradiations has been in use, many thousands of such irradiations have been carried out, and the errors have been very few.

## TYPICAL RADIOACTIVE TRACERS

### (i) *Phosphorus* 32 *and Iodine* 131

Of the requests for chemically separated radioactive materials, the vast majority are for phosphorus 32, of half-life 14·3 days, and for 8-day half-life iodine 131. Both are used for metabolic studies, and therapeutically for a very limited number of diseases. Between them, the methods of preparation illustrate most of the processes used in handling curie amounts of active isotopes without added carrier, and where micrograms of the active material have to be separated from hundreds of grams of target compound and prepared in a very high state of purity. They illustrate also the point that what can be done in unshielded beakers at activity levels of about a millicurie must be done in an almost completely remotely-controlled apparatus when activity levels are several hundred times higher. Of the two radio-isotopes, phosphorus 32 has the more widespread applications, for, besides its medical uses, it is of great interest in biochemical and agricultural research.

Phosphorus 32 emits β-particles of maximum energy 1·7 MeV,[1] and no γ-rays. It is prepared by irradiating ordinary sulphur, the isotope of mass number 32 absorbing a neutron and then emitting a proton, so that it is converted to phosphorus 32 by an (n,p) reaction. It is necessary to extract the phosphorus 32 from the sulphur, and to convert it into the chemical form of dilute orthophosphoric acid.

The process used at Harwell [15] for extraction of phosphorus 32 is nearly the same chemically as that used at Oak Ridge, U.S.A., but the apparatus is considerably different.

Two to six 300 g blocks of irradiated sulphur are taken at a time, and stripped of their wrappings by means of specially shaped cutters and tongs operated through Perspex sheet. Each block contains about 0·3 curie of phosphorus 32. They are then melted, and extracted at about 130° C in 0·2N nitric acid in a Pyrex glass vessel, which is itself inside a stainless steel pressure-pot that can be rocked to stir the contents. After a few hours, most of the phosphorus 32 appears in the aqueous phase as orthophosphate ion. On cooling, the sulphur block is removed and discarded. The solution consists of the required orthophosphoric acid, unwanted nitric acid, and possibly some sulphuric acid which would contain radioactive sulphur 35 and inorganic and organic impurities.

All handling of the solution is behind Perspex screening, and solutions are drawn up into small reservoirs and pass from vessel to vessel by gravity feed. First, the solution is drawn up into a reservoir from which it passes through a glass filter into a vacuum-jacketed distillation flask (figure 6), where the volume is reduced from 1500 to about

[1] MeV = Million electron volts.

80 ml. It is drawn into a second reservoir, and flows down into an appropriate reactor. Here it is held above a sintered glass disk by compressed air, while about 20 mg of lanthanum hydroxide is precipitated in it. This adsorbs the phosphorus. Nitric and sulphuric acids remain in solution as ammonium salts, since the lanthanum hydroxide is precipitated with ammonia. After redissolving, reprecipitating, and refiltering, the precipitate is dissolved in hydrochloric acid, and passes down into a small evaporator heated by xylene vapour. It is evaporated several times nearly to dryness, water being added each time, to reduce the hydrochloric acid content. Organic matter is destroyed by hydrogen peroxide, and the residue is taken up in about 0·1N hydrochloric acid.

The solution is sucked up to a third reservoir, and allowed to flow down through a column of cation-exchange resin and thence into a final evaporator. It is now free from radioactive and non-radioactive inorganic impurities, but it may have picked up a little organic matter from the resin column. The solution is therefore evaporated nearly to dryness, and treated two or three times with a few drops of very pure 100-volume hydrogen peroxide. It is finally evaporated down once with triple-distilled water, and made up to a stock solution, which is standardized in terms of radioactive content per millilitre, and is also spectrographically analysed.

The various orders for phosphorus 32 have by now been made up as part of the weekly dispensing list, and the solution is dispensed, sterilized, and sent out. Phosphorus 32 solutions must be very carefully kept and dispensed, as any dust in the solution will adsorb a large proportion of the activity. Moulds or bacteria growing in the solution would rapidly metabolize phosphate into other phosphorus compounds, and thereby render the solutions useless. If solutions are kept dust-free, slightly acid ($p$H $\simeq$ 3), at an activity level of more than ten millicuries per millilitre, and sterilized before dispatch the activity is preserved in the correct chemical form.

Iodine 131 is still mainly produced from tellurium. One of the natural tellurium isotopes, $Te^{130}$, undergoes the (n,$\gamma$) reaction to $Te^{131}$, which is converted by $\beta$-decay into iodine 131. The isotope occurs also in good yield as a product of uranium fission, and fission-product iodine 131 will probably replace that from tellurium in Britain during 1952, as it has already done in the U.S.A.

For the present [16], powdered tellurium metal is irradiated in aluminium cans, each containing about 150 g. After two weeks' irradiation at a flux of $8 \times 10^{11}$ neutrons per $cm^2$ per second, each can contains about 350 millicuries of iodine 131. The tellurium from one can at a time is dissolved in a chromic-sulphuric acid mixture. The iodine goes into solution as iodic acid, and the tellurium as telluric acid. The solution is cooled and reduced with oxalic acid. With this reagent, the iodate ion is reduced to elementary iodine, the remaining components of the system remaining in solution. The iodine 131 can be distilled off, and trapped in alkaline sodium bisulphite as iodide, but the solution is too impure for most purposes as it contains traces of tellurium, oxalic acid, and chromic ion. It is purified by destroying the oxalic acid with permanganate, and then just discharging the last of the permanganate in sulphuric acid solution with the minimum quantity of oxalic acid, and distilling a second time into alkaline bisulphite. The second distillate is very pure indeed, and is evaporated down to a solution which is standardized for radioactivity and analysed spectrographically as usual, before being dispensed. The entire process of preparing and dispensing iodine 131 must be carried out behind lead shielding about 2 inches thick (figure 6).

The problem of keeping stock solutions of iodine 131 in the correct chemical form is as important as is the similar problem with $P^{32}$. The action of $\beta$- and other ionizing radiations on water is such as to produce oxidizing conditions. Iodine 131 at about 20–25 millicuries per millilitre, in solution in the chemical form of iodide, may, in the course of a few days, be partially converted to elementary iodine. This radiation effect can be minimized by storing solutions with a slight excess of bisulphite at a $p$H of 7–9, and at not more than 8–10 millicuries per millilitre.

There is usually a small amount of ordinary iodine in tellurium used for $I^{131}$ production. Even when, as target material, tellurium is chosen which contains as little inactive iodine as possible, the fresh solution of iodine 131 contains about 0·5 microgram of inactive iodine per millicurie, or about a hundred inactive iodine atoms to every atom of iodine 131.

(ii) *Carbon* 14

Carbon 14 is the radio-isotope most used for the labelling of organic compounds in biochemical and similar research. It has a long half-life—about 6000 years—and emits only $\beta$-particles of low energy, with a maximum of about 0·15 MeV. It is particularly easy to see in the case of carbon

14 why the radioactive material must first be prepared in one chemical form, and then synthesized into the correct compound for subsequent use.

The nuclear reaction used in the preparation of carbon 14 is the (n,p) reaction on nitrogen 14. Nitrogen is usually irradiated in the chemical form of potassium nitrate. The carbon 14 appears mostly in the chemical form of carbon dioxide, and can be extracted by dissolving the irradiated nitrate in dilute nitric acid and sweeping out the gases with $CO_2$-free air. The carbon 14 can then be precipitated, in a solution of a mixture of potassium and barium hydroxides, as barium carbonate. Carbon 14 prepared by this method is accompanied by a large proportion of inactive carbon of uncertain origin. It is quite usual to send out material at an isotopic abundance of 5 per cent. carbon 14.

The syntheses of important organic intermediate compounds from labelled carbon dioxide, and a few more extensive syntheses, are carried out by a group of chemists at the radiochemical centre at Amersham. Syntheses are usually carried out with about one millicurie of $C^{14}$ per millimole of compound. This is sufficient for most purposes, but can be increased in cases where the dose given to an animal, for example, has to be kept small and yet contain as much activity as possible.

### BIOCHEMICAL USES OF TRACERS

It is in the field of biochemistry that labelled compounds have been used with most spectacular success. The number of ways in which they can be used is very large, and is already far beyond the scope of a single review article. Among them are typical uses which may here be described very briefly.

The simplest use of radioactive tracers is in following an element irrespective of its state of chemical combination. The gross metabolism of elements in animals may be important, in order to see whether they are retained, and particularly whether they are localized, in the body, or whether they are rapidly excreted. The health hazard due to a radio-isotope of the element may depend more on its behaviour in the body than on its radioactive properties. The distribution of radioactivity can be studied on the large scale using counter techniques, and on the small scale with autoradiographs. The study of the distribution of iodine 131, sodium 24, and phosphorus 32 has been used for diagnosis, and often as a preliminary to the use of massive doses of the isotope in therapy.

Reactions in extremely complicated chemical systems can be studied with the aid of labelled compounds. In living systems, for example, a labelled compound may be administered, and activity extracted from the system in an unknown chemical form. Evidence for the chemical nature of this radioactive metabolite may be obtained by mixing with it a pure sample of the compound which it is suspected to be, and then attempting to separate pure compound and radioactive residue by such physical means as repeated crystallization [17] and chromatography [18]. If the two are not separated by any one process, their chemical identity is probable but not strictly proved. However, the greater the number of different processes which are tried and fail, the less likelihood is there that the radioactive residue is not the same chemically as the pure compound.

There is no doubt that the method of combined chromatography and radioactive measurement [18, 19, 21] is already the most flexible and satisfactory means of resolving, identifying, and estimating the amounts present of a number of the metabolites of a single administered labelled compound.

### THE STUDY OF PHOTOSYNTHESIS

The availability of carbon 14 has made possible remarkable advances in the chemistry of photosynthesis. Calvin [21] and his co-workers have developed techniques whereby algae such as *Chlorella*, or even green leaves, may be grown in the normal way, and then studied in an apparatus in which they can be illuminated for definite times in the presence or absence of carbon dioxide labelled with carbon 14.

The classical analytical methods for studying the chemical forms into which carbon 14 passes were soon found to be inadequate, and the method of combined two-dimensional paper chromatography and autoradiography was used extensively for the identification and semi-quantitative estimation of compounds.

Calvin carried out photosynthesis with ordinary inactive carbon dioxide, then stopped the gas-flow, injected carbon dioxide labelled with $C^{14}$ as aqueous sodium bicarbonate, and continued photosynthesis for a period which might be as short as five seconds or as long as many minutes, stopping the process by dropping the contents of the reaction vessel into hot alcohol. It was hoped by reducing the period of photosynthesis to find the compound or compounds into which carbon dioxide was first fixed, afterwards lengthening the

period and following the conversion into other compounds.

The success achieved was remarkable. By degrading compounds by known methods, or modifications of known methods, it was possible to study the appearance of activity even in individual carbon atoms of molecules as a function of time of photosynthesis, to deduce sequences of reactions, and confidently to postulate intermediates in reaction cycles. The potentialities of the radioactive tracer method are well illustrated by this type of study.

### DILUTION TECHNIQUE

If a small, known amount of a labelled compound A* at known specific activity is put into a chemical system large by comparison, of which there is an unknown amount of a component A the same chemically as A*, and thoroughly mixed, then the labelled compound will be diluted by the unknown amount of A. A sample of the mixture is taken, and the A in it is thoroughly purified and its specific activity re-measured. If $y$ is the unknown amount of A in the system, and $x$ the known amount of A* originally added at a specific activity $C_0$, and if the final specific activity is $C$, then it is easily seen that:

$$y = \left(\frac{C_0 - C}{C}\right)x.$$

This gives a means of measuring $y$ when the amount of sample finally taken is unknown. All that is necessary is an efficient chemical purification and accurate measurement of specific activities. The technique has many applications in the study of biological and other systems.

### KINETIC MEASUREMENTS

The variation with time of the specific activity of a compound is really the variation with time of the concentration of activity in that particular chemical form. Studies of the specific activities of compounds containing a radioactive element can give a great deal of information in many systems, biological and otherwise. In the biological field, these have been reviewed by Radin [20].

### INDUSTRIAL APPLICATIONS OF RADIOACTIVE ISOTOPES

For some years, the applications of radioactive methods to industrial problems lagged far behind the work done on biochemical systems. Recently, however, many industrial applications have become established practice. These may be divided into two main classes. Firstly, there are those which are adaptations of the biological applications: generally simple in method, but on a large scale, and sometimes requiring the preparation of large sources of active material. Secondly, there is a class of applications in which the radiations from radioactive substances are required for their physical properties alone.

The first class is represented by such applications as the labelling of the junction between two different grades of oil being pumped along a pipeline, the labelling material being γ-active so that its movement can be observed from outside the pipeline. Another application is the location of leaks in telephone cable sheathings, by pumping radioactive methyl bromide vapour labelled with bromine 82 into the cable, and detecting the activity in the neighbourhood of the leak [22]. Large-scale studies of ventilation-rates in buildings can be studied by observing the diminution of the activity of a radioactive rare gas due to continuous dilution with fresh air.

Wear can be followed by making one part of an engine radioactive and, after running it for a time, measuring the radioactive debris in the lubricating oil. The advantages of radioactive technique in this kind of study is that particular parts of an engine may be investigated, and the time taken for a wear measurement is a very small fraction of that which would be necessary for the usual life-test.

There are three main industrial uses of the radiations from radioactive substances. Firstly, γ-active sources are used for the radiography of castings, welds, and mechanisms in non-destructive testing. X-ray machines of suitable voltage are bulky and expensive, and the increased exposure which has to be given with a γ-ray source is partly compensated by the fact that it is often possible to radiograph a whole group of castings at once, with the same source. Radium and radon were used extensively as γ-ray sources, but they have the disadvantage of being expensive in the one case and short-lived in the other. A range of pile-produced γ-sources has been made available to industry, and has found immediate acceptance. The isotopes of greatest use have so far proved to be cobalt 60 of half-life 5·3 years and giving γ-rays of 1·17 and 1·33 MeV; tantalum 182 of half-life 117 days and similar γ-energies; and iridium 192 of half-life 70 days and giving γ-radiation of about 0·5 MeV. Other sources are being developed for similar purposes. A recent review [23] of the position explains how it is now possible to select

the most suitable source for a particular purpose.

The second industrial application of radiation is the non-contact gauging of the thickness of sheet materials. If a source of β-active material is placed below a moving sheet of paper, the proportion of β-rays absorbed in the paper will depend on the thickness of the paper, expressed as mg per $cm^2$. If a standard piece of paper is placed between a second source and a second ionization chamber, the two chambers can be connected in opposition to give a null instrument. Any departure in either direction from standard thickness of the paper being manufactured is registered instantaneously, and can be corrected on the machine.

β-particles are scattered by materials, the efficiency of back-scattering increasing markedly with atomic number. If the β-source and detector are placed on the same side of a sheet of material, the back-scattered β-rays will be a measure of the thickness of that material, providing it is thin relative to the absorption half-thickness of the scattered radiation. If a material is coated with a substance of widely different atomic number, then the back-scattering from the material will be modified by the coating, and a measure of the coating thickness obtained. For example, lacquers on steel will reduce the back-scattering, while tin on steel will increase it. The limiting sensitivity for measuring thickness of tin, of the order of $10^{-4}$ inch on steel, is $10^{-6}$ inch of tin.

Heavier-gauge sheeting than can be measured with β-particles may be measured with γ-absorption gauges or γ-back-scattering gauges, but there is a range of thickness which is too thick for β-ray measurement and too thin for convenient γ-ray measurement. New sources of very low energy γ-rays are being developed in order to solve this particular problem [24].

Thickness-gauges employing these principles have been developed in Britain and are available for industrial and other uses.

The third application of radiation is in the dispersal of static electricity in industrial processes. There are many processes in which insulating materials are handled, and static charges may build up until handling becomes very difficult, or even until the charges constitute a fire hazard. Radioactive sources can be used to ionize the air locally, and cause the charges to leak away to earth. In the United States, α-emitting materials are much used for this purpose, but such sources have disadvantages. β-sources of appropriate energy and half-life are quite suitable for the elimination of static charges, and thallium 204 of half-life 3 years and maximum β-energy 0·7 MeV will cope with mild charges. More serious static charges will make necessary the development of more intense sources of β-active material of long half-life and moderate energies, housed in very safe containers, so that even in the event of a factory fire the radioactive hazard will be slight.

During the last decade a number of methods of exploiting the properties of radioactive materials have been developed. It would be rash to say that no new basic methods will appear for some time, but the present effort lies in developing new sources and ways of using the pile, and adapting the methods already developed in the biochemical field to the solution of other problems in both academic and applied science.

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# Lysogenic bacteria, I

ANDRÉ LWOFF

Bacteriophages and viruses are of exceptional biological importance in that they apparently represent the simplest forms of living matter and are therefore of special interest in relation to the problem of the origin of life itself. In one respect, however, their properties seem to be paradoxical, for they can apparently flourish only within living cells—often specific cells—and it is therefore difficult to see how they could have come earlier in evolution. They are also of practical significance in relation to the conquest of bacterial infections.

## INTRODUCTION

Bacteriophages are particles which generally exhibit all the properties usually considered to be characteristic of ultraviruses: virulence, i.e. an infective and pathogenic power; a small size—less than 1300 A; and the property of being able to propagate only within a cell, often specific. In the so-called lysogenic bacteria, however, the bacteriophage occurs as a type of potential virus, a probacteriophage, which is neither infective nor pathogenic. In some cases, the probacteriophages may develop into bacteriophages which, if liberated by bacterial lysis, are able to infect and lyse sensitive bacteria belonging to the same or related species. Lysogenic bacteria pass on by heredity the power of producing bacteriophages. Each contains a specific particle endowed with genetic continuity, which apparently behaves like a normal particle but can, under certain conditions, be transformed into a virus. This curious fact should serve to awaken our interest. Attention is specially drawn to the proviso 'under certain conditions'; its significance and full import will be elucidated in the second article.[1]

## BACTERIOPHAGES—ORDINARY SYSTEMS

To introduce the principles of lysogenesis to those who are not familiar with microbiology, we begin with the so-called ordinary systems. By this we understand a system which consists of the pair: sensitive bacterium + virulent bacteriophage. These systems are called 'ordinary,' as they have represented, and still represent, the favourite material of the phagologists. There is nothing depreciatory about the term.

It is known that the bacteriophage is a spherical particle whose diameter varies between 200 and 1000 A; it consists more or less entirely of desoxyribonucleic protein. It is sometimes provided with a threadlike appendix which, for no scientific reason but merely because of its shape, is called a tail. If a bacteriophage penetrates into a sensitive cell, the cell ceases to grow. Under favourable conditions, and if the surroundings provide the necessary nourishment, lysis of the bacterium takes place after about twenty minutes, with the liberation of about a hundred bacteriophages.

Research on bacteriophage action necessarily began with these ordinary systems, carefully selected because of their interesting properties, such as the dramatic character of their relations with bacteria. These systems represent, however, the last stage of an evolutionary process. Bacteriophage action in ordinary systems is, in fact, an extraordinary case, a kind of showpiece differing considerably from lysogenesis, which, as will be shown, must be considered as the phylogenetically primitive form of bacteriophage action.

Because of the usually fatal issue of the encounter between bacteria and bacteriophages, certain specialists on ordinary systems refused to grant to lysogenic systems the right of even a theoretical existence, because of their abnormally harmless character. The lysogenic systems have, however, survived this arbitrary condemnation; they have proved the reality of their existence, and have converted their judges to a more flexible conception of bacteriophage action.

## THE HISTORY OF LYSOGENESIS

It will be useful to give a short survey of the development of our knowledge on this subject, limiting ourselves to important contributions.

The term lysogenic bacteria was introduced as soon as the bacteriophages which they produced were called lysogenic units. It would have been clearer and more logical to call them phagogenic bacteria. Lisbonne and Carrère discovered in 1921 that a strain of *Escherichia coli* (= *Bacterium coli*) produced a bacteriophage which lysed certain strains of dysentery-causing bacilli of the genus

[1] Part II will appear in our July issue.

*Shigella*. These strains would have been of little interest had they been, as F. d'Hérelle suggested, a vaguely balanced mixed population of slightly sensitive bacteria and mildly virulent bacteriophages. In 1925, however, J. Bordet showed that in a lysogenic strain each bacterium produces a lysogenic colony. He concluded that the bacteriophage is included in the hereditary pattern of the bacterium. As lysogenic bacteria are insensitive to the bacteriophages which they themselves produce, Bordet further concluded that the bacteria secrete bacteriophages without being damaged by them. The meaning of this so-called secretion will be considered later.

Next, the work of F. M. Burnet and his collaborators provided very important contributions to our knowledge of lysogenic bacteria:

1. Lysogenic systems can easily be obtained by mixing non-lysogenic bacteria with appropriately selected bacteriophages. Under these conditions, the majority of the infected bacteria are lysed. A small proportion, say of the order of $10^{-7}$, resist, multiply, and produce clones which prove to be lysogenic. (A clone is the aggregate of individuals produced from a single individual by vegetative or asexual reproduction.)
2. The bacteriophages produced from these experimental lysogenic strains are identical with the original bacteriophages. Lysogenic bacteria thus perpetuate a specific particle.
3. Experimental lysis of lysogenic bacteria does not liberate bacteriophages. From this observation, F. M. Burnet and M. McKie concluded in 1929 that the bacteriophage perpetuates itself in lysogenic bacteria in a non-infective form.
4. In a culture of lysogenic bacteria, only a small proportion of the bacteria liberate bacteriophages.

Finally, according to these Australian workers, lysogenic bacteria contain in their hereditary make-up a unit which is potentially capable of liberating bacteriophages. To cause the liberation of bacteriophages, its spontaneous activation is required. They assumed that this action is spontaneous and follows the exponential law.

The fundamental discovery of the perpetuation of a virus in the form of a non-infective and non-virulent modification thus dates from 1929. It was more than fifteen years before this non-infective phase in the life-cycle of the ordinary bacteriophage was rediscovered; the idea was then extended to the viruses of encephalomyelitis and influenza. The researches of F. M. Burnet and M. McKie had met with general indifference, and had been forgotten. It seems that silence is the best and most effective weapon to be used against pioneers: in his book 'Virus as Organism' (1946) even F. M. Burnet himself does not mention his earlier work.

Meanwhile, research on lysogenic bacteria proceeded. In 1932, den Dooren de Jong discovered lysogenesis in *Bacillus megatherium*. He showed that the spores of the bacillus gave rise to lysogenic clones. Some years later, E. and E. Wollman established that lysozyme does not liberate bacteriophages from lysogenic *B. megatherium*, thus confirming the conclusions of the Australian authors with regard to the existence of a non-infective phase of the bacteriophage.

Finally, in 1939, J. Northrop determined the increase in the number of bacteriophages and the production of gelatinase during the growth of a culture of lysogenic *B. megatherium*. He obtained curves which appeared to be parallel; in his opinion this justified the conclusion that the bacteriophage is an enzyme, and that this enzyme is secreted during bacterial growth.

## LIMITATIONS OF STATISTICAL INTERPRETATION

Let us assume that in a developing culture the ratio of the number of bacteria to the number of bacteriophages remains constant, and that the value of the ratio is unity. This result can be achieved in two different ways:

(*a*) Each bacterium liberates a bacteriophage every time it divides.

(*b*) During the time-interval between two divisions, a given percentage of bacteria liberate numerous bacteriophages, e.g. one in 200 bacteria liberates 200 bacteriophages. In this case the theoretical rate of growth would be reduced by 0·5 per cent. This is difficult to observe, as the measurement of growth-rates is not possible to an accuracy nearer than 5 per cent. The investigation of a bacterial population thus leaves no means of choosing between hypotheses (*a*) and (*b*).

If lysogenic specimens of *B. megatherium* are brought into contact with the bacteriophages which they produce, the latter are adsorbed but the bacteria nevertheless continue to develop. Lysogenic bacteria are evidently resistant to the bacteriophages which they themselves liberate. In ordinary systems, the mutants which are resistant to a given bacteriophage do not adsorb it, and

from a purely practical point of view they could be described as impermeable. The resistance of a lysogenic bacterium is obviously of a different character, for here the bacterium is penetrated by the bacteriophage; this resistance represents a kind of immunity. It is thus not surprising that the conception of J. Bordet, who stated that lysogenic bacteria which liberate bacteriophages without being harmed by them must actually secrete them, has been generally accepted.

Indeed, how could it be conceived *a priori* that only one of the phases in the life-cycle of the bacteriophage in a lysogenic bacterium should represent a pathogenic character? No reasoning by analogy, no mathematical analysis of the behaviour of a population, could lead to this conclusion. In order to discover the truth, and to recognize the way in which lysogenic bacteria liberate the bacteriophages which they produce, it is sufficient to study a single individual bacterium, but necessarily one only.

### LYSOGENESIS OF A SINGLE CELL

In order to set a single bacterium to work, the arrangement shown in figure 1 was used. This consists of a plastic chamber containing a rheostat and a thermo-regulator. It also contains a microscope and two micromanipulators. One, the Fonbrune micromanipulator, holds a micropipette, and serves to take out the bacteria, to transfer them individually, one per drop, and to take out samples of the medium. The other, the Zeiss-Peterfi micromanipulator, serves to hold and move a Pasteur pipette which is previously filled with liquid. The opening of the pipette can be moved to the centre of the field of the microscope, and it is also possible to inject the contents of the micropipette, held by the micromanipulator, into the Pasteur pipette. Once this is charged, it is treated as an ordinary pipette; its contents could, for example, be transferred to a tube of agar. The culture medium used in the micromanipulations is put on a slide in drops of different sizes (figure 2); the small droplets have a diameter of about 100 μ. Following the classical technique, this slide is then inverted over a clean slide, the remaining space being filled with paraffin oil, in order to prevent the evaporation of the droplets. This also allows the diffusion of oxygen and the movement of the micropipette.

*Experiment* 1. A *B. megatherium* is removed from a culture of lysogenic bacteria. It is successively passed through five large drops to clear it from free bacteriophages which might be present. It is then injected into a droplet of nutrient medium (figure 4). After each division, one of the daughter bacteria is removed with a little liquid. The removed bacterium is transferred to a dish containing nutrient agar previously inoculated with a strain of *B. megatherium* sensitive to the bacteriophage produced by the lysogenic strain. This operation is repeated up to the nineteenth division. At this stage, the two daughter bacteria are removed, and immersed in the liquid of the droplet.

Each of the twenty dishes (figure 3) showed a single area of lysis surrounding a colony. This means that each of the bacteria has given birth to a colony which has produced bacteriophages, i.e. it has produced a lysogenic clone. Had there been a liberation of bacteriophages in the droplet during the nineteen divisions, areas of lysis would have appeared on the dish. There were, however, none except the area surrounding the lysogenic colony. Lysogenesis has thus been preserved through nineteen divisions in the absence of any exterior bacteriophages. If, in this experiment, lysogenesis had been perpetuated by the action of external bacteriophages, the latter would from the start have been present inside the bacterium under test. Had they then been equally distributed among the daughter bacteria during the nineteen divisions, it would follow that the original bacterium contained more than $2^{19}$, i.e. more than 524,288 bacteriophages; this is mechanically impossible, because of the dimensions of the bacteriophage and the bacterium. Lysogenesis therefore perpetuates itself in an endomicrobial manner, which means that it is hereditary.

This experiment also shows that lysogenic bacteria multiply without producing bacteriophages. The liberation of bacteriophages, in contrast to the synthesis of constitutive enzymes, does not necessarily accompany growth and normal bacterial division.

*Experiment* 2. A filament of four bacteria is washed and transferred into a droplet, where it multiplies. Samples of the droplet are taken at regular intervals (figure 5), and are spread over the sensitive bacterium. None of the dishes shows the presence of bacteriophages. When there are 64 bacteria in the droplet, lysozyme is injected. The bacteria are lysed. The whole droplet is then removed and poured on to the sensitive bacterium. No area of lysis is seen. Lysogenic *B. megatherium* does not in fact contain any infective particles. Yet in every sufficiently large population of bacilli there are always free bacteriophages to be found. How are they liberated?

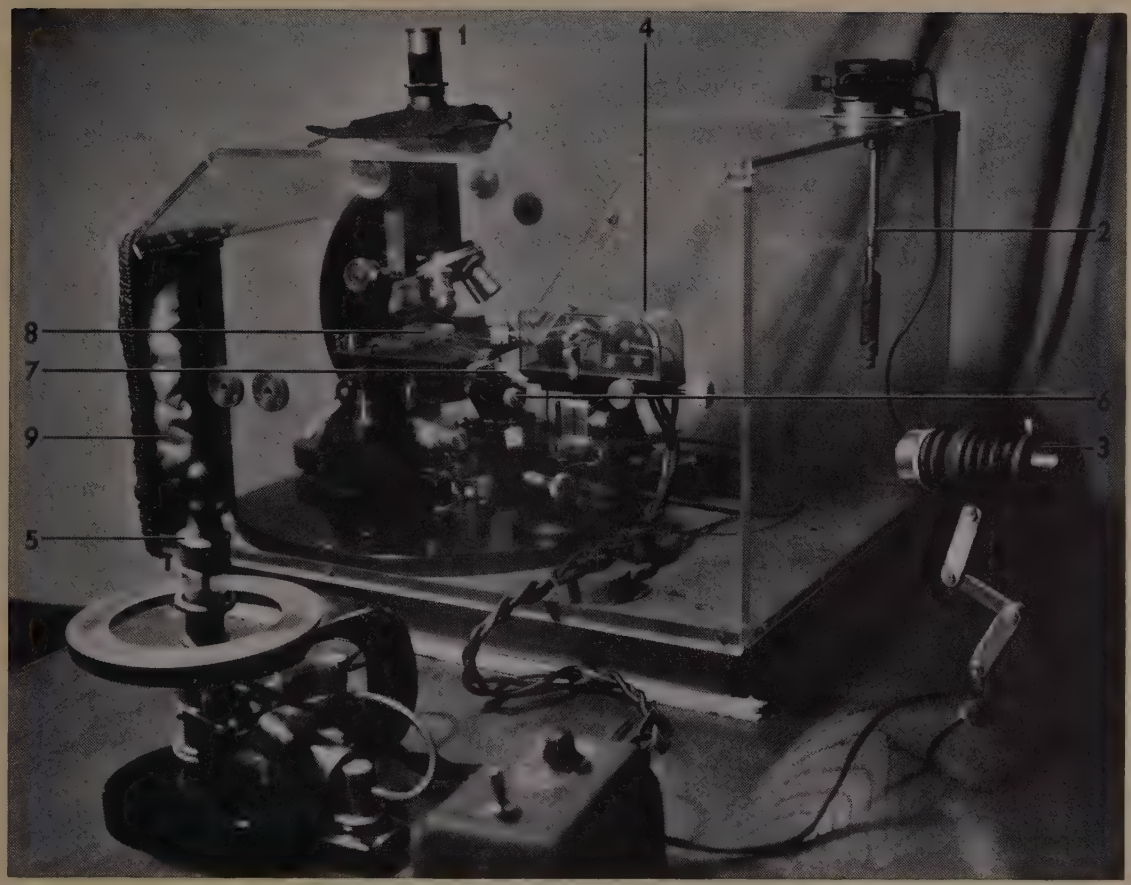


FIGURE 1 – *Heated chamber used for the micromanipulations.* (1) *Microscope,* (2) *thermo-regulator,* (3) *lamp for the illumination of the microscope,* (4) *Fonbrune's micromanipulator,* (5) *lever controlling* 4, (6) *Zeiss-Peterfi's micromanipulator,* (7) *Pasteur pipette,* (8) *oil chamber,* (9) *one of the curtained openings (right) which allow the hands to be introduced into the apparatus.*

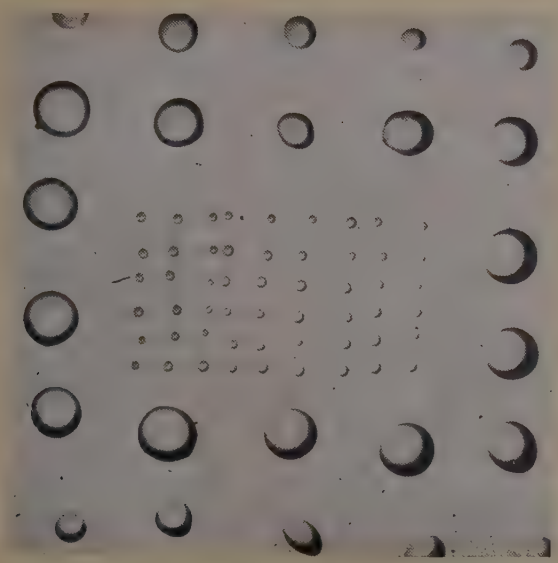

FIGURE 2 – *Photograph of droplets of medium on the slide. The small droplets have diameters of* ca. 100 μ.

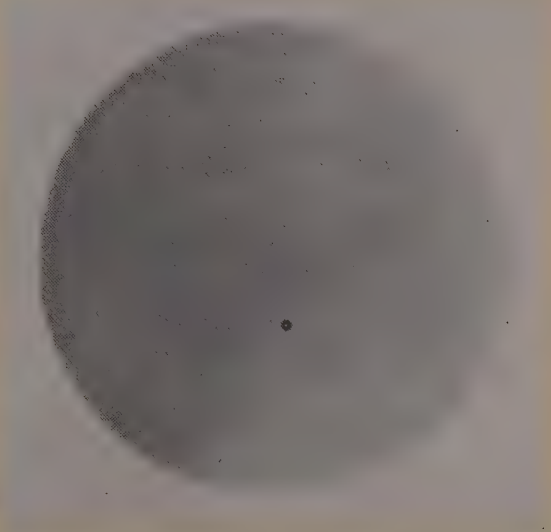

FIGURE 3 – *The uniformly grey background on the Petri dish represents the culture of sensitive bacteria. An area in which sensitive bacteria have been lysed can be seen surrounding a colony. This colony has developed from a single germ, representing the nineteenth generation in the droplet. (A. Lwoff and A. Gutmann.)*

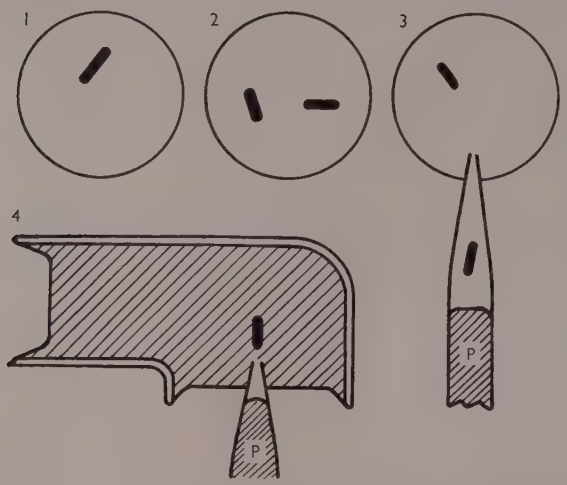


FIGURE 4 – *A washed bacterium is placed in a droplet* (1) *where it divides* (2). *One of the daughter bacteria is removed* (3) *and injected into a Pasteur pipette* (4). *This operation is repeated nineteen times.* P: *Paraffin oil.*

*Experiment* 3. A filament of two bacteria is washed and transferred into a drop of fresh medium (figure 6). The bacteria divide. At the 65th minute there are eight bacteria and no bacteriophages. Between the 83rd and 89th minute four bacteria can be seen under the microscope to disappear successively. This disappearance is very rapid: the observer watches a bacterium, and suddenly within less than a second it disappears, leaving no visible trace. There were, however, 579 bacteriophages in the drop where the lysis of the four bacteria occurred. Numerous similar observations have been made, and bacterial lysis was frequently observed. It could be shown that three minutes before lysis no free bacteriophages were present. The bacteriophages are liberated by the bacterial lysis, and by the lysis only, lysis of one bacterium liberating 100–200 bacteriophages.

Thus, in a population of lysogenic bacteria, some bacteria multiply without liberating bacteriophages: these bacteria perpetuate the lysogenic strain. Others are lysed and liberate bacteriophages; these bacteria manifest the lysogenic character. The perpetuation of lysogenic bacteria and the production of bacteriophages are incompatible.

Lysogenic bacteria thus perpetuate a specific particle, the probacteriophage, which is non-infective and non-pathogenic, and which apparently behaves like a normal particle. But this probacteriophage represents a potentially lethal character, which lies entirely in its hypothetical future. If the probacteriophage uses its latent powers by developing into a bacteriophage, the bacterium is killed.

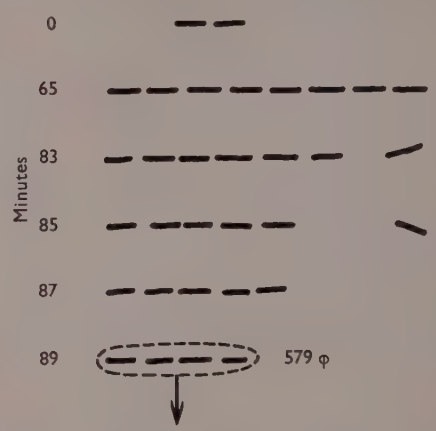


FIGURE 6 – *Bacteria dividing in a droplet. Four of them are then lysed. The four surviving bacteria are eliminated;* 579 *bacteriophages are found in the droplet.*

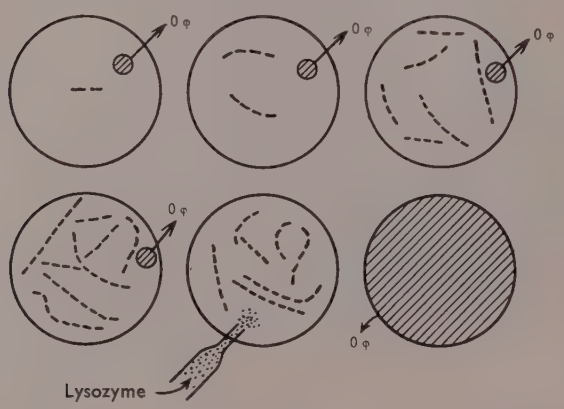


FIGURE 5 – *Bacteria developing in a droplet. No bacteriophages are found in test samples* (0 φ). *After injection of lysozyme and bacterial lysis the whole droplet is spread out over the sensitive strain; no bacteriophages are found.*

Lysogenic bacteria can, as has been shown, adsorb the bacteriophages they have themselves produced, at least in small doses, without suffering any damage. The bacteriophage is not pathogenic. Multiplication of the probacteriophage as such is compatible with the survival of the host bacterium. The probacteriophage is not pathogenic; the pathological effect is produced by the process of development of the probacteriophage into a bacteriophage.

It should be added that, so far, no example is known in which lysogenic bacteria secrete bacteriophages while they continue to multiply.

Theoretically, this phenomenon may be possible. Its actual occurrence could be proved only by observation of isolated bacteria in droplets. Any conclusions drawn from an interpretation of statistical data are without real value and represent mere hypotheses.

### RECOVERY (LOSS OF LYSOGENIC POWER)

Lysogenic bacteria perpetuate a specific particle endowed with genetic continuity. How is this particle included in the hereditary pattern of the microbe? What is its degree of co-ordination with the microbial protoplasm? Is it attached to a particle of the bacterial organism, for example a chromosome, or does it possess a certain degree of independence?

Cases of recovery of lysogenic bacteria have been described, but without an analysis of the factors concerned. However, N. A. Clarke and P. B. Cowles (personal communication) bred *B. megatherium* in a synthetic medium to which citrate had been added. They found that after 75 sub-cultures the strain had lost its lysogenic character and, in addition, had become sensitive to the bacteriophages which were produced before recovery. We have repeated and confirmed this important experiment. Lysogenic strains were subjected to rapid sub-culture in a synthetic medium with or without addition of oxalate. After the 27th sub-culture, no more bacteriophages were produced by the two strains, and they had become sensitive. What do these results mean? It is probable that the rate of multiplication of the probacteriophage in bacteria bred in a synthetic medium is smaller than the rate of multiplication of the bacteria themselves. This might entail a progressive decrease of the number of probacteriophages and their final disappearance. In any case, the bacteria lose their lysogenic character, but why do they become sensitive?

A mixture of bacteria in the state of recovery, and of bacteriophages, in the ratio of one bacterium to five bacteriophages, was seeded on to a layer of nutrient agar. All the bacteria became infected, and the majority were lysed. Some, however, developed, and produced clones which were found to be lysogenic.

It may be assumed that in a population of sensitive non-lysogenic bacteria there are always resistant, or rather immune, mutants, i.e. bacteria into which the bacteriophage can penetrate and where it is transformed into a probacteriophage, and which perpetuate the probacteriophage. In a population of sensitive bacteria, such as the one considered above (i.e. in absence of bacteriophages), natural selection definitely favours sensitive germs, as they form a majority. On addition of bacteriophages, only the immune germs will develop and produce a lysogenic strain. In such a lysogenic population back-mutations—immune → sensitive—will allow the development of probacteriophages into bacteriophages, and the mutants will be lysed. The statement that, in a lysogenic population, only the immune will persist, is a truism. If, however, the population loses its probacteriophage, the sensitive mutants of the strain, which is now non-lysogenic, will not be destroyed, for there is now no production of bacteriophages. They will become dominant by natural selection, as they are favoured in relation to those that are immune.

In soil, the natural habitat of *B. megatherium*, all the strains isolated so far have been found to be lysogenic. As soon as bacteriophages exist in natural surroundings, only the immune germs can survive and, as we have seen, with *B. megatherium* bacteriophage-immunity is equivalent to lysogenesis. This applies also to numerous lysogenic species whose resistance, contrary to that of the ordinary bacteria, is not due to a modification of the surface layer which prevents penetration by the bacteriophage. The resistance of lysogenic bacteria is due to properties of the bacteria which allow only multiplication of the probacteriophage, and prohibit its development into a bacteriophage.

### THE PROBLEM

We have endeavoured to present a certain number of well-established facts concerning lysogenesis, but there remain numerous questions as yet unanswered. In particular, why do certain bacteria in a lysogenic population multiply normally, while others lyse with liberation of bacteriophages? We shall deal with such questions in the sequel.

NOTE. The author has been enabled to perform his research on lysogenic bacteria by a grant of the National Cancer Institute of the National Institutes of Health (Public Health Service of the U.S.A.).

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# Identical cattle twins and colour inheritance

JOHN HANCOCK

Monozygotic twins, each genetically identical, have proved of great value in the study of human genetics, for they provide a unique means of assessing the influence of factors other than heredity. Similar studies in animals are of comparatively recent date, primarily because the superficially less striking individual characteristics of animals make the diagnosis of genetic identity difficult. During the last six years some three hundred monozygotic cattle twins have been studied at Ruakura Animal Research Station in New Zealand.

Twins have played an important part in helping to solve the age-long problem of the relative importance of inheritance and environment as factors causing differences between human beings. In principle, the method employed is as follows. There are two types of twins: monozygotic (uniovular, one-egg, or identical) and dizygotic (diovular, two-egg, or fraternal). Twins of the first type are the result of the splitting of a single fertilized ovum, and are thus genetically identical. Twins of the second type develop from two separate ova, and are therefore no more similar, in the genetical sense, than full sibs. Any differences in physical or mental traits between the members of monozygotic twin sets can be ascribed to environmental influences entirely, whereas differences between the members of dizygotic twins are due partly to environment and partly to inheritance. A comparison of the magnitude of differences found within the two classes of twins provides a direct, precise test of the relative influence of nature and nurture.

Workers in animal research were naturally encouraged by the success of the twin method in human biology to use a similar approach. There existed also a great need for homogeneous experimental material, especially in a slowly maturing and highly variable species such as cattle.

As early as in 1924 [1] the first set of monozygotic cattle twins was described. Further progress, however, was slow, owing—at least partly—to the *a priori* assumption that it would be difficult to distinguish between monozygotic and dizygotic twins, on account of the morphological uniformity existing within cattle breeds.

Kronacher [2] first established the rules for the diagnosis of zygocity in cattle twins. He employed the similarity method evolved by investigators of human twins. Recently, the present writer [3] showed that this method, slightly altered, can yield very precise results. The test, as applied by him, consists of a critical although entirely subjective comparison of all visible characteristics; it aims at providing an answer to the question: Are the differences of such a kind, and is their sum sufficiently small, to justify the assumption that the twins are monozygotic?

In general, the usefulness of a trait as an aid in twin diagnosis is enhanced by (i) increasing number of genetical factors influencing the trait, (ii) decreasing effects of non-germinal factors, (iii) increasing ability by the operator to measure or perceive differences. Hair and skin pigmentations fulfil these conditions to a varying degree. By 1933 [4], nineteen different hair-colour genes had been postulated, and many factors have been added later. The expressions of the colour genes are in general relatively little influenced by environment, but, as it is easy to perceive even small differences visually, the problem of diagnosing zygocity lies in deciding the extent to which each colour effect may vary under the influence of non-germinal factors.

In the course of the twin-collection work during the last six years at Ruakura Animal Research Station, New Zealand, nearly one thousand like-sexed twin sets have been examined. Of these, nearly three hundred sets have been judged to be monozygotic. In the light of the experience gained at Ruakura, it is intended in this paper to examine the usefulness of various hair and skin colours as criteria of zygocity. It will also be shown how the study of twins has yielded some new information about the inheritance of the above characteristics.

Ibsen's [4] nomenclature will be followed, but his gene symbols will be used to describe the phenotypic expression of a gene as well as to

designate the gene itself. It should be understood that almost every statement about the colour effect of a gene is tacitly qualified by the proviso 'if the action of other genes does not interfere.'

### 1. RED (R)

Red (R) is present in all cattle except albinos [4]. The red colour does not always show, because R is hypostatic[1] to (i.e. masked by) many other non-allelomorphic genes. There are many shades of red coat colour, ranging from the dark plum red seen in some Shorthorns to an almost pure white occurring frequently in Jerseys. The members of a set of monozygotic twins show no differences in the shade of red if treated uniformly. Indeed, only when the twins have been submitted to markedly contrasting environments have differences in shade of red been noted. Dizygotic twins, on the other hand, often show pronounced differences in this colour. Thus it seems that most, if not all, of the varying shades of red occurring in a herd of cows must be ascribed to differences in inheritance. For the present purpose, it does not matter whether the differences are caused by a number of genes specific for red, or whether a number of dilution factors operate.

The pleiotropic[2] effect of R on skin pigmentation has not been clarified thoroughly in previous work. According to observations at Ruakura, it appears that the brown pigment of an R animal extends to the whole skin surface, and not only to the nose and eyelids, as previously stated [4].

### 2. BLACK EXTENDER (E)

In Ibsen's terminology, all cattle are genetically black (B), but the black pigment is extended to all hairs only if the animal also carries the factor E. Three sets of black monozygotic twins at Ruakura, which were heterozygous for E according to their pedigrees, were uniformly red or brownish at birth but became jet black after having shed their birth coat. A fourth set turned dark grey and remained this colour. It thus seems obvious that E in the heterozygous condition is not absolutely epistatic[3] over red (R).

### 3. BLACKISH ($B_s$)

Generally, the black hair of this colour pattern is concentrated only in certain areas. However, there are very great variations in the extent to which the black hair covers the surface. At one extreme a $B_s$ animal may appear totally black, while at the other extreme black hairs may be present only in the switch of the tails. All gradations occur between these extremes. Similarly treated monozygotic twins show hardly any differences in this characteristic, while dizygotic twins are often very unlike. The $B_s$ colour pattern is not a reliable criterion of zygocity if the members of a twin set have been subjected to widely different environments. It has been observed at Ruakura that the extent of black hair in animals kept indoors fades in comparison with that of their co-twins kept outside. Lactation is another factor which lightens the coat colour. Except under these conditions, it seems that all variations in the blackish pattern must be explained in terms of genetical differences. The genes which produce the various shades of red coat colour do not seem to affect blackish hair, for red of any shade may be found in combination with any degree of blackish hair.

The pleiotropic effect of $B_s$ on the colour of the skin has not been described adequately in previous work. As the skin pigment pattern is the distinguishing mark between a $B_s$ animal and other types fairly similar phenotypically but genetically different, a description is given here. For the most part, the colour of the skin is black, but a strip of brownish skin runs from the lower jaw down the throat, brisket, belly, and udder, continuing along the whole length of the escutcheon over the vulva and anus and along the inside of the tail. In many cases, however, it seems that a break in the brown skin occurs in the region of the throat, stretching as far as half-way down the dewlap. The whole inner surface and the lower portion of the outer surface of the ears are also brown-skinned.

Characteristically shaped black pigmented areas are frequently present on the brown skin inside the ears (ear streak) and on the ano-vulvar region (a-v spot).

The whole of this skin colour-pattern, including the black marks on the brown area, is laterally symmetrical and is absolutely similar within sets of monozygotic twins, while dizygotic twins often show marked differences. This indicates that all variations observed must be explained in terms of genetical differences.

The relationship between the intensity of blackish hair due to the $B_s$ gene, the ear streak,

[1] Hypostatic: the absent one of two characters which are not allelomorphs. An allelomorph or allele is one of two (or more) dissimilar factors which occur at corresponding positions on homologous chromosomes.

[2] Pleiotropic: affecting several characters.

[3] Epistatic: the predominant of two characters which are not allelomorphs.

and the a-v spot is not yet clear. In a sample of 108 $B_s$ animals of pure-bred and high-grade Jersey stock, it was found that 25 lacked the ear streak, while the a-v spot was missing in only two animals. When the cows were graded according to the degree of blackness on a 1–14 scale and the a-v spot on a 0–7 scale, the following results were obtained:

| Degree of blackish hair | 1 | 2 | 3 | 4 | 5 | 6 | 7–14 |
|---|---|---|---|---|---|---|---|
| No. of animals .. | 19 | 17 | 14 | 16 | 13 | 16 | 13 |
| Average relative size of a-v spot | 2·8 | 3·1 | 3·6 | 3·5 | 3·7 | 4·6 | 4·5 |

There was thus a marked tendency for lighter animals to have smaller a-v spots, but this relationship was not by any means perfect. Many very dark animals had small spots, and *vice versa*. It was found similarly that the ear streak was missing in 42 per cent. of all animals classed 1 and 2 on the scale for blackness, while only 16 per cent. of the animals darker than class 2 lacked this trait. However, some very dark animals were also devoid of ear streak.

### 4. BLACK EARS ($b_e$)

Observations of skin and hair colours in the Ruakura twin herd necessitate the proposal of a new factor, $b_e$. The skin pigment pattern of a $b_e$ animal differs from that produced by the $B_s$ gene inasmuch as only the skin of the udder, belly, brisket, and the upper two-thirds of the inner surface of the ears is brown, while the rest of the skin is black as far as can be ascertained. This pattern is remarkably uniform from animal to animal, and monozygotic twins do not show any within-set differences.

The hair of the inner fringe of the ears is generally jet black (figure 2*a*), but this is thought to be due to interaction between the genes $b_e$ and $B_s$ rather than to the action of $b_e$ alone. There are at present two sets of monozygotic twins at Ruakura which show the typical $b_e$ skin colour pattern, but in which the colour of the hair fringe inside the ears is a darker version of the main body colour instead of the usual black. Judging by their coat colour, these animals do not carry the $B_s$ gene.

Out of 140 cows in a herd of pure-bred and high-grade Jerseys, nineteen showed the $b_e$ pattern. Breeding records kept at Ruakura suggest that 'black ears' is determined by a simple recessive gene.

### 5. BRINDLE ($B_r$)

Brindle describes a colour consisting of irregular stripes of black hair on a red background. The $B_r$ gene can act only in the presence of the gene for blackish hair ($B_s$) [4]. Until recently, the variations of brindle colour have received little attention, in spite of the marked variations that occur from animal to animal. The lightest type shows only a few bluish streaks on an otherwise brown-pigmented muzzle, while at the other extreme an animal may appear almost jet black, owing to the density of the black stripes. The very light brindles can easily be mistaken for reds.

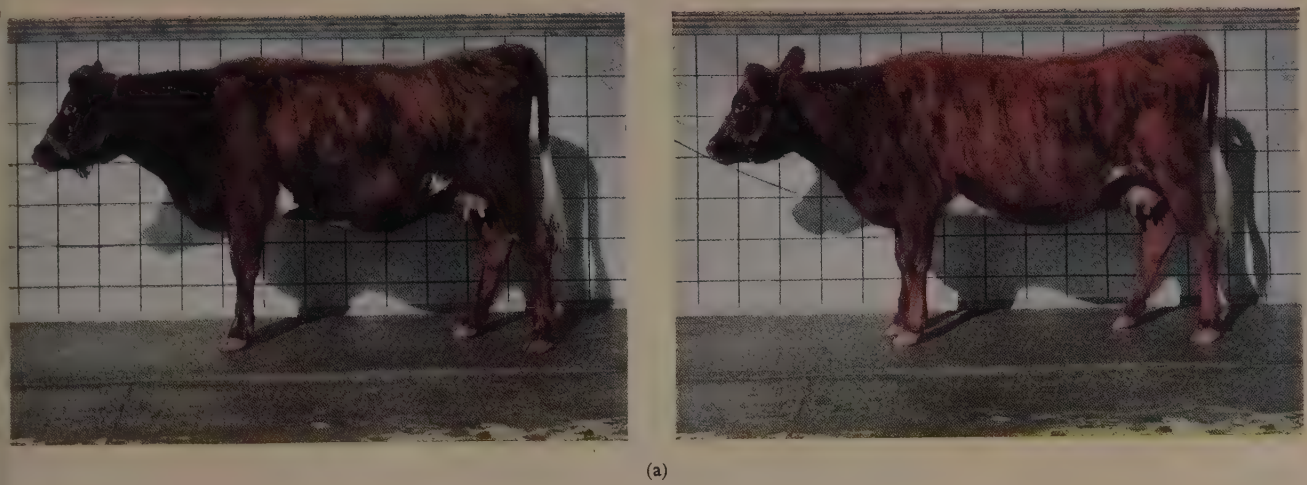
As one side of an animal often differs to some extent from the other in regard to brindling, it is not surprising that monozygotic twins show some within-set differences. The three sets of brindle twins in figures 1*a*, *b*, and *c* illustrate only a small portion of the range of between-set (genetical) differences, while the set in figure 1*a* shows the greatest within-set (non-genetical) variations observed in any twins at Ruakura. It seems that a great many factors must be postulated to explain the genetic variations occurring in the brindle colour.

The effects of the $B_r$ gene on the pigmentation of the skin have not been noted previously. The skin of a $B_r$ animal is brown with bluish streaks of varying intensity, whether the animal is $B_s$ or $b_e$. The ear streak and the a-v spot common in $B_s$ animals are totally inhibited in the presence of $B_r$.

The factor E, which extends black pigment to all hair, is not always completely epistatic to $B_r$. A set of twins at Ruakura which, according to their pedigree, were heterozygous for E, appeared to be jet black, but showed on closer examination an unmistakable brindling. As their skin was black, it may be assumed that $B_r$ does not affect the skin pigment produced by E. A similar case has been described by S. Berge *et al.* [5].

### 6. RECESSIVE WHITE SPOTTING (S AND s)

S causes an animal to be entirely pigmented (self or self-coloured). Its allelomorph (s) inhibits the hair and skin pigment in certain areas. Both inherited and non-germinal factors influence the extent of the white areas. However, it has been estimated [6] that over 90 per cent. of the variations are due to inheritance. Observations on Ruakura twins bear out this contention. The within-set differences which measure non-germinal variations are generally no greater than those occurring between the two sides of the same animal (see figures 4*a*, 4*b*). The between-set differences are very great, ranging from almost wholly white animals to those which show white in the tips of the tails only.

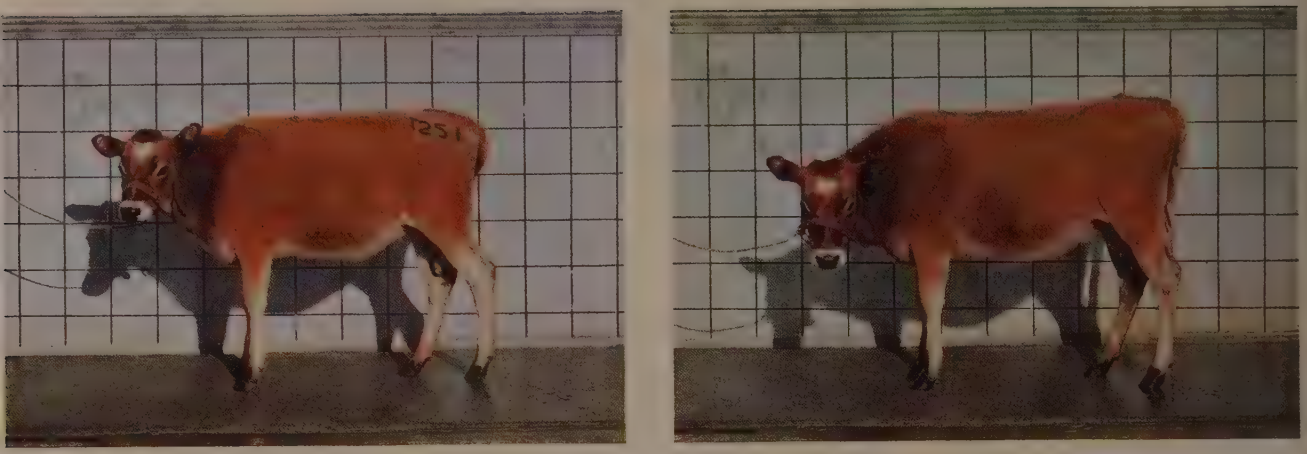


(a)

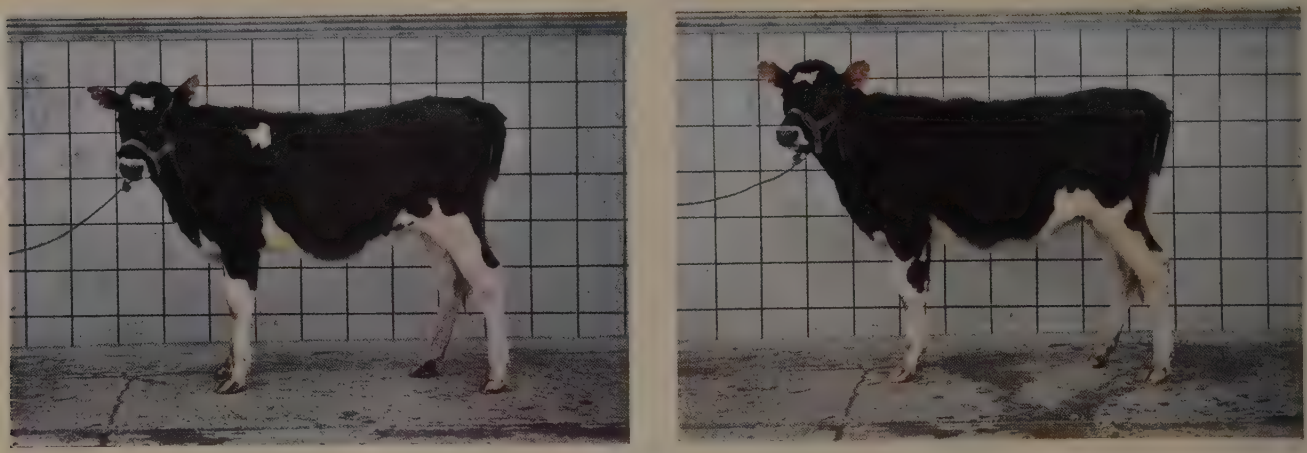
(b)

(c)

FIGURES 1*a*, *b*, and *c* – *Three sets of brindle identical twins.*




(a)

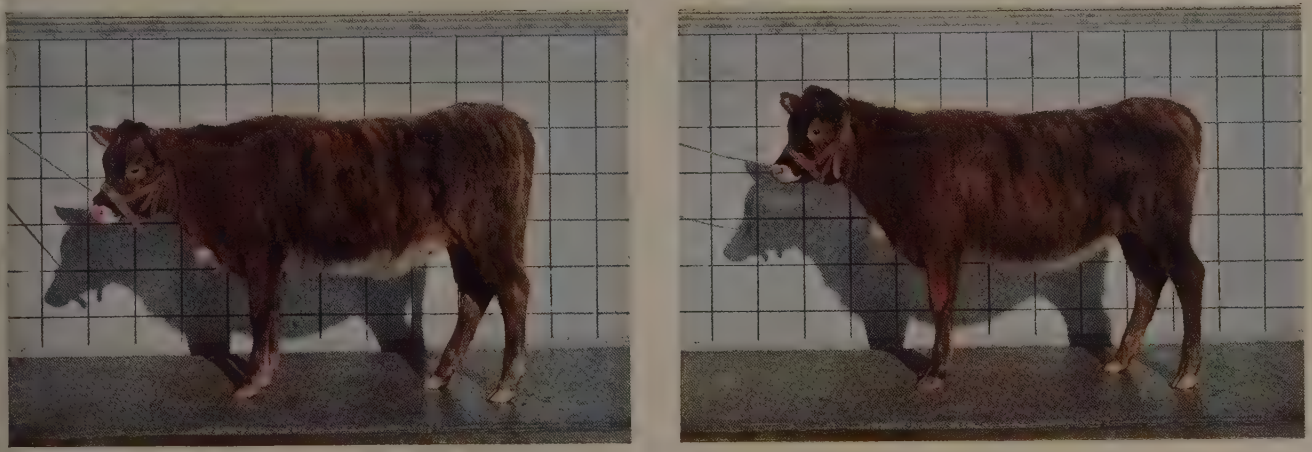


(b)

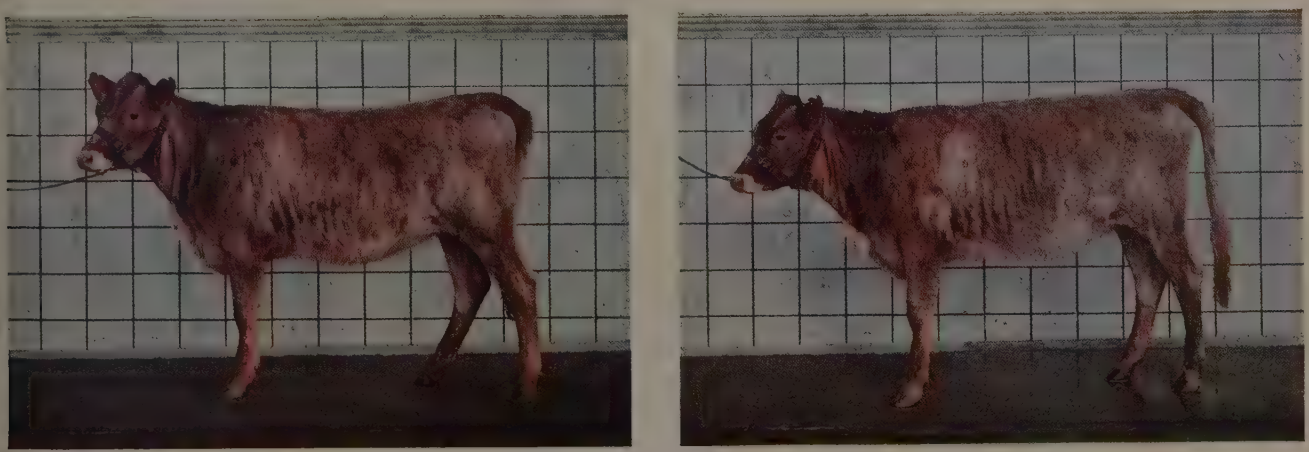
(c)

FIGURES 2*a*, *b*, and *c* – *Three sets of identical twins, showing various degrees of white spotting.*

(a)



(b)



(c)

FIGURES 3*a*, *b*, and *c* – *Three sets of identical twins, showing different degrees of roaning.*

(a)

(b)

FIGURES 4*a* and *b* – *Right and left sides of the members of a set of white-spotted twins.*

FIGURE 5 – *The udders of a set of identical twins, showing a high density of skin spots.*

The three sets of monozygotic twins in figures 2*a*, *b*, and *c* illustrate the between-set and within-set differences occurring in the lower third of the white spotting range. Briquet *et al.* [6] stated that it is necessary to postulate at least four pairs of genes in order to explain the genetical differences in white spotting. They measured the gene effects as the percentage of white visible when the animals were viewed from the side. Nevertheless, many animals classified as self-coloured on this scale would be white spotted on the underline.

### 7. ROAN (N)

The roan colour effect is caused by white hairs interspersed among pigmented ones. Roan is determined by the gene N in heterozygous state (Nn). An animal homozygous for N is wholly white except for pigmented hairs on the ears [4].

Previously, little attention had been paid to degrees of roan coloration. Roan varies continuously, from a colour which seems to be made up from approximately equal numbers of white and pigmented hairs, to a colour in which the white hairs are so sparse that the animals appear to be self-coloured. As monozygotic twins, compared with fraternal twins, show relatively small differences in degree of roan, it must be assumed that inherited factors are responsible for the greater part of observed variations. The three sets of twins in figures 3*a*, *b*, *c* bear out this point. Only variants on the light portion of the roan scale were chosen for the illustration, as less intense roans might appear self-coloured in photographs. Ibsen [4] postulated a modifying factor (rm) which turns a genetically roan animal (Nn) into red. It seems necessary, however, to assume the existence of a whole series of modifiers in order to explain all the observed between-set differences.

Observations based on twins indicate that the gene N, whether in homozygous or heterozygous condition, has no effect on skin colour. Thus, the colour of the skin of an Nn or NN animal depends on whether it is at the same time black (E), red (R), blackish ($B_s$), black ears ($b_e$), or brindle ($B_r$). White spotting (ss) can be detected in animals which are homozygous for N (and therefore pure white) by the presence of unpigmented skin areas. Contrary to a previously held view [4], NN is therefore not epistatic to white spotting.

An entirely different type of roan has been noted in two sets of monozygotic twins, and also in a few other cattle. It occurs only in white-spotted (ss) animals which at the same time show pigmented skin spots on otherwise unpigmented skin areas. The white hairs on these skin spots are interspersed with pigmented ones, producing a spotted-roan effect. The hair on the areas not covered by white spots is, however, non-roan. As the presence or absence of this trait is strictly concordant in monozygotic twins, it may be assumed that this type of roan is determined by inherited factors.

### 8. PIGMENTED OR BLACK SKIN SPOTTING ($P_s$)

This factor is mentioned here merely to draw attention to the manner in which its expression differs from that of a new skin spotting factor described below. $P_s$ causes black skin spots to occur on otherwise brown skin areas [4]. At the present time, there are no twins at Ruakura showing this characteristic, but it has been noted in a few cows in the grade Jersey herd.

### 9. BROWN AND BLACK SKIN SPOTTING ($P_b$)

There is a type of skin spotting which appears so characteristically different from the effect of the $P_s$ gene that it has been found necessary to ascribe it to a new factor ($P_b$). The spots produced by the gene $P_b$ are visible only on otherwise unpigmented skin, i.e. on skin areas which are affected, for instance, by recessive white spotting. The colour of the spots is either black or brown, depending on the other genes present. In black animals (E), all spots are black, but in $B_s$ and $b_e$ animals they are black or brown, depending on whether they fall on normally black or brown skin areas. In red (R) and brindle (B*r*) animals, the spots are brown and brown-brindled respectively.

The presence or absence of spots is strictly concordant in monozygotic twins. The size, density, and position of the spots vary from one animal to another, but as the differences observed between sets of twins are generally greater than those occurring within sets, it may be assumed that both the degree and the presence of this type of spotting depend on inherited factors. Spotting of the $P_b$ type is so common in Jersey and cross-bred Jersey cattle that it may be assumed that a dominant gene is involved.

In some instances, the density of the spots may be so great that the areas of skin covered by white hair, due to the gene s, are wholly black or brown instead of partly unpigmented. The udders of the set of monozygotic twins shown in figure 5 illustrate a case in which this condition is nearly realized.

### 10. DISCUSSION AND CONCLUSIONS

An attempt has been made to show that most

of the variations which occur in coat and skin colours of cattle are due to genetical differences. The genes with specific and graduated colour effects are quite numerous and well established, but they do not in themselves suffice to explain the bewildering number of distinct colour patterns observed. A great many patterns are actually the products of the interactions between two or more independent genes, rather than the result of a single gene action.

It can be readily understood that very numerous patterns can be evolved, especially in cattle of the Jersey breed, by the combination of the various modifiers of red, blackish, and white spotting, together with the genes for black ears and pigmented skin, and other factors which have not been described in this paper. In fact, so many are the possible combinations that it would be difficult, if not impossible, to find in a finite population of Jersey cattle two animals with exactly the same colour pattern. It is therefore not surprising that over 90 per cent. of the dizygotic twins examined at Ruakura can be distinguished by the differences they show in hair and skin colour alone, even when the examination is made at birth, when many colour effects are only poorly developed.

In regard to the inheritance of colour in general, it may be emphasized that the key to many hair colour genes lies in their pleiotropic effect on skin pigmentation. Many blackish ($B_s$) or black ear ($b_e$) animals, for instance, could not be distinguished from black (E) animals except by their characteristic skin pigment pattern. Similarly, many blackish animals would be taken for red if hair colour were the only criterion. There are genes which dilute the red colour to such an extent that it would not be possible, in some cases, to decide whether an animal is white-spotted, except by the presence of areas of unpigmented skin. By similar means it is possible to detect white spotting in animals which are wholly white-haired owing to the action of the roan factor (N) in homozygous condition.

Knowledge of this kind provides the basis for breeding cattle with various combinations of hair and skin colours. For instance, a breed with white hair on black skin to suit tropical conditions could be evolved by combining the white hair of homozygous roan Shorthorns with the black skin of the Aberdeen Angus.

Another possible way of achieving a similar result would be the combination of a great density of skin spots ($P_b$) with the factors for black extension (E) and roan (N) in homozygous condition. This, however, would be a more difficult task than the first alternative.

It is conceivable that a more complete knowledge of colour inheritance will throw some light on the relationship between various breeds of cattle. Judging by the coat colour, it seems, for instance, that the Jersey is a closer relation to the zebu (*Bos indicus*) than the Brown Swiss, although the two latter breeds, superficially at least, have more features in common (drooping ears and large dewlaps).

Observations of monozygotic twins at Ruakura have made it possible to postulate at least two new factors, $b_e$ and $P_b$, affecting coat and skin colours in cattle. The factor $b_e$, which causes black hair on the inside fringe of the ears in conjunction with $B_s$, is essentially a skin-pattern factor. The factor $P_b$ is a skin-spotting factor which produces either black or brown spots or both, according to the genetic composition of the animals.

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# Effects of radiations and radiomimetic drugs

E. BOYLAND

Recent research has brought to light several marked similarities between the biological effects of certain vesicants and carcinogenic compounds and those of X-rays and similar ionizing radiations. Both kinds of agent, for example, may inhibit tumours and yet be carcinogenic; both may reduce the white cell count of the blood. These noteworthy effects, which are of great potential significance in the treatment of cancer, may, despite their very different origins, be due to a common action in changing nucleic acid or other cell constituents.

The treatment of disease, including cancer, by X-rays began very soon after the discovery of this type of radiation by Röntgen in 1895. Radium, too, was used soon after its discovery. At first, the attendant dangers were not realized—the first cancer due to exposure to X-rays was described by a German radiologist, Frieben, in 1902 [9]—but increased experience, care, and skill in using X-rays and radium have reduced the risks of this type of therapy. The result of treatment is, however, probably dependent on specific cell damage, which is manifested in a wide range of biological effects. In recent years, very similar changes have been induced by the application of certain chemical substances in place of the ionizing radiations. The changes induced are so similar to those caused by radiation that such substances were called radiomimetic by P. Dustin [8]. Some of the effects produced by substances of this type, and by radiations, are shown in table I.

TABLE I

*Both Ionizing Radiations and Radiomimetic Drugs:—*

1. Inhibit growth of tumours or the whole body.
2. Induce cancer at site of action.
3. Produce chromosome damage (figures 1–4).
4. Produce mutations.
5. Cause delayed death with similar *post mortem* changes.
6. Cause erythema and inflammation.
7. Destroy viruses.
8. Depolymerize nucleic acid *in vitro* (figure 7) and probably also *in vivo*.
9. Destroy white cells of the blood, causing leucocytopenia.
10. Reduce blood clotting ability, probably owing to reduction of the number of circulating thrombocytes.
11. Cause local greying of hair (figures 5 and 6).
12. Inhibit the development of immunity which involves the production of antibodies when an antigen is administered.
13. Destroy complement (a normal blood constituent necessary for lysis of foreign red blood cells).
14. Inhibit sulphydryl enzymes, such as triosephosphate dehydrogenase.
15. Produce blisters on skin.
16. Cause haemoconcentration owing to withdrawal of water from blood.
17. Cause nausea and vomiting analogous to radiation sickness, and lesions in the intestinal *mucosa*.
18. Cause delayed hyperglycaemia.
19. Produce foetal abnormalities in pregnant animals.
20. Cause a negative nitrogen balance, owing either to increased breakdown of protein or to decrease in protein synthesis.

As the twentieth century proceeded, X-rays and rays from radium were used for many technical and scientific processes. Muller studied the occurrence of mutations in the fruit fly *Drosophila*, and found that exposure to X-rays caused a great increase in their incidence. Some years later, Muller and Painter showed that treatment with X-rays caused microscopically visible damage to chromosomes of dividing cells. The chromosomes of cells previously irradiated often exhibit specific abnormalities such as fragmentation, stickiness, and bridging (see figures 1 and 2).

Ionizing radiations also produce profound effects on the blood picture of animals or men; a decrease in the white cells, particularly lymphocytes, occurs after relatively small doses of radiation.

The vesicant or blistering effect of mustard gas, *bis*-β-chloroethyl sulphide, was described in the nineteenth century (Meyer, 1887 [15]), and this substance was used extensively in chemical warfare in 1917 and 1918. During the last war, mustard gas and other vesicants were studied, such as the nitrogen mustards (particularly methyl *bis*-β-chloroethyl amine, code sign HN2, and *tris*-β-chloroethyl amine, code sign HN3). Their ability

to reduce the white cell count (or leucopenic action) was frequently observed, and because of this action the nitrogen mustards were tried in the clinical treatment of leucaemia and diseases of the lymphatic glands. The leucopenic action of nitrogen mustard is similar to that of irradiation. Other radiomimetic effects of mustard gas and nitrogen mustards include the increase in the incidence of mutations in *Drosophila*, first reported by Auerbach, Robson, and Carr [1], and the induction of specific chromosome damage described by Darlington and Koller [6] (see figure 3). The chromosome damage produced by mustard gas resembles that due to X-rays.

The nitrogen mustards and mustard gas itself, like radiations, are carcinogenic, for they have produced tumours in animals (described by Boyland and Horning [4] in England, and by Heston [13] in U.S.A.). The fact that they have been described as anticarcinogenic is in keeping with the apparent paradox that many of the means used to treat cancer are themselves carcinogenic.

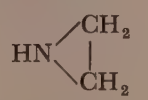
The mustards are only a few of the many known chemical carcinogenic agents. The carcinogenic hydrocarbons, which are related to constituents of coal tar, inhibit growth of cancer and of normal tissue, as was shown by Haddow. Many different aromatic carcinogenic compounds have been found to inhibit the growth of normal and malignant tissues, to cause mutations in *Drosophila* (Demerec, 1948 [7]), and to cause specific chromosome damage (Koller—personal communication). Thus changes which are associated with specific and limited chromosome damage have been seen with the aromatic carcinogenic compounds. An interesting example was the use of the most potent carcinogenic hydrocarbon, 9:10-dimethyl-1:2-benzanthracene, in the clinical treatment of leucaemia.

One radiomimetic effect which can readily be demonstrated is the local greying of hair, examples of which are shown in figures 5 and 6. This effect in mice has been described following X-irradiation [12], following nitrogen mustard [3], and following implantation of plutonium [14]. The change appears to be permanent, for mice injected with nitrogen mustard have retained their white patches for nearly three years. Because the change is discontinuous and permanent it might be a somatic mutation, analogous to that suggested in the transformation of normal into cancer cells. Investigation of the nature of the change by histological techniques has, however, not supported this suggestion.

The action of X-rays possibly depends upon the free hydroxyl radicals liberated from the water in the system. If this were the case, then the effect of X-irradiation should be reproduced by free hydroxyl radicals. Free hydroxyl radicals can be produced in aqueous solution by adding a reducing agent such as ferrous sulphate to hydrogen peroxide. Injection of hydrogen peroxide and ferrous sulphate (Fenton's reagent) into coloured mice has produced the typical greying of hair.

Many other effects have been induced by radiations and radiomimetic drugs, as shown in table 1, but not all these effects are produced by all the agents. Thus the carcinogenic hydrocarbons and related substances do not readily produce blisters or greying of hair, and they cannot take part in reactions where solubility in water is necessary. The only effects which can be considered useful are the inhibition of tumour growth and the treatment of leucaemia and similar diseases, on which a great deal of research has been carried out.

The simple nitrogen mustard $HN_2$, or methyl *bis*-β-chloroethyl amine, has been used extensively for the treatment of Hodgkin's disease. It is effective but very toxic; it causes nausea and must be given by intravenous injection. Haddow, Kon, and Ross (1948, [11]) have tested a large number of aromatic chloroethylamines, and American workers have tested a number of aliphatic derivatives. The most satisfactory of the aromatic compounds was the β-naphthylamine derivative, *bis*-β-chloroethyl β-naphthylamine, a substance which has had extensive clinical trial in the treatment of Hodgkin's disease. This substance can be given by mouth and does not cause nausea or vomiting. The most interesting of the American compounds were *tetra*-β-chloroethyl diamines. The work seemed on the whole to indicate that the active compounds contained at least two reactive chemical centres, but recently some activity has been found with monofunctional compounds such as ethyleneimine:



(*cf.* Biesele and Stock, 1950).

The apparent necessity for two reactive groups led Goldacre, Loveless, and Ross (1949, [10]) to suggest that the substances acted as cross-linking agents in the chromosomes. The cross-linkages formed would interfere with division of the chromosomes, so that abnormalities would be

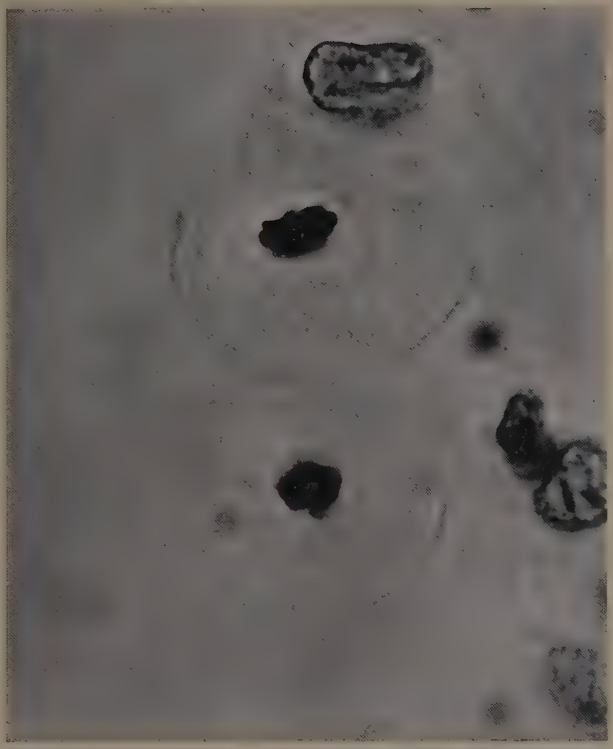


FIGURE 1 – *Photomicrograph of dividing cells of normal tumour (Walker rat carcinoma) cells, showing the end of cell division with two daughter nuclei containing the coalesced chromosomes.*

FIGURE 2 – *Dividing cells of Walker carcinoma 24 hours after irradiation with X-rays (300 r). The two sets of daughter chromosomes show bridges which will prevent separation of the nuclei, and fragments of separated chromosomes.*

FIGURE 3 – *Dividing cells of Walker carcinoma 24 hours after treatment of the rat with nitrogen mustard (1 mg methyl bis-β-chloroethyl amine per kilogram body weight). Similar abnormalities are produced by X-rays (cf. figure 2).*

FIGURE 4 – *Dividing cells of Walker carcinoma from a rat 24 hours after treatment with 1 g urethane per kilogram body weight. Fragments of chromosomes can be seen between the two nuclei.*

[*Figures 1–4 (× 2100) are due to Dr P. C. Koller of the Chester Beatty Research Institute.*]

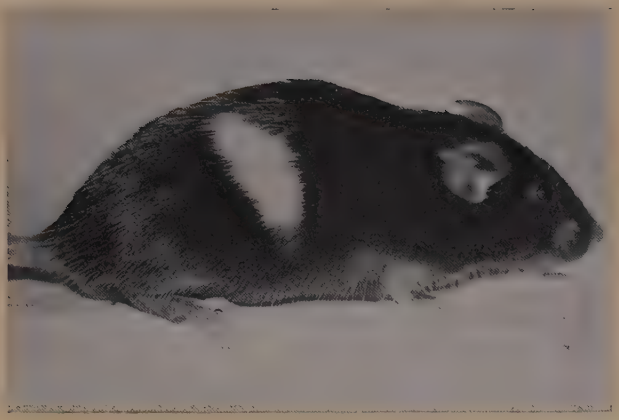


FIGURE 5 – *Black mouse four weeks after irradiation of a part of the skin with X-rays* (1000 *r*). *The irradiated area is permanently depigmented, although the hair continues to grow.*

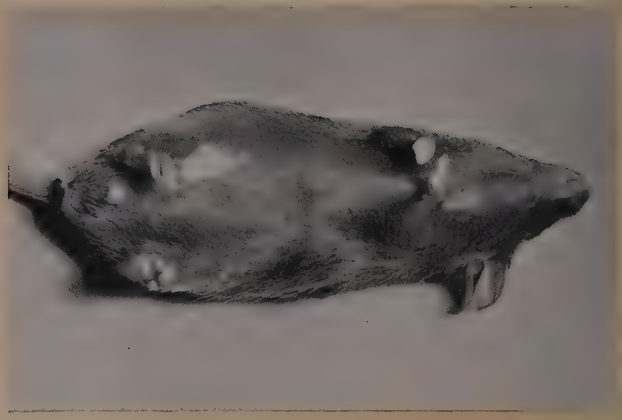
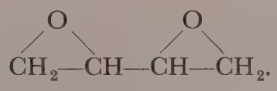


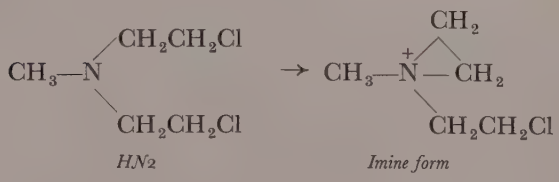
FIGURE 6 – *Black mouse four weeks after intradermal injection of* 0·001 *mg nitrogen mustard.*

formed at cell division. In investigation of this hypothesis, a number of known cross-linking agents were tried, including the diepoxides such as butadiene diepoxide:

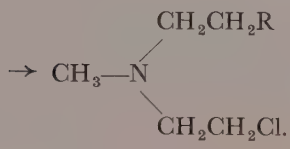


This substance has been found to inhibit tumour growth and to break chromosomes, and has induced cancer. Although it is of little use in clinical treatment of disease, it indicates that other reactive groups capable of alkylating acids can replace the chloroethyl groups of the mustard gas compounds.

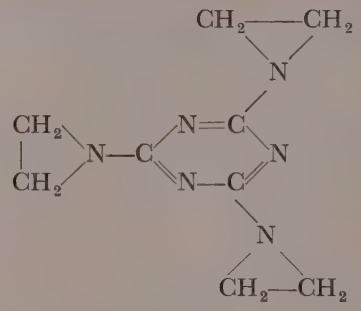
The aliphatic nitrogen mustards probably react through intermediate formation of an ethyleneimine ring, e.g.



*HN2* *Imine form*



The fact that nitrogen mustards act as ethyleneimines and possibly as cross-linking agents made it seem likely that a triazine triethylene-imine:



described as a cross-linking agent for wool by the *Farbwerke Hoechst*, would be an active compound. The substance was tested independently in London, Manchester, and New York and was found to be very active; it is now used in the clinical treatment of lymphadenopathies. It does not cause nausea, and can be given by mouth. It has the disadvantage of causing a greater fall in haemoglobin than the original nitrogen mustard.

In some of the effects produced, it is possible to calculate the doses of compounds and radiation which will produce equivalent effects. In general, a dose of 0·2 mg nitrogen mustard ($HN_2$) per kilogram bodyweight, i.e. a concentration of 0·2 mg per litre, which is one-millionth molar ($M \times 10^{-6}$), is equivalent to irradiation with 100 r of X-rays. Although urethane will produce some of the effects of nitrogen mustard (see figure 4), nitrogen mustard is about 10,000 times as active as urethane in producing chromosome breaks in experimental rat tumours. It is possible that X-rays produce their effects by decomposing water to liberate free hydroxyl radicals within cells. An exposure of 100 r could produce a concentration of about $0{\cdot}3 \times 10^{-6}$ M of free hydroxyl

radicals. Thus equivalent effects are produced by $0{\cdot}3 \times 10^{-6}$ M free hydroxyl radicals (or other products of irradiation) and by $1 \times 10^{-6}$ M nitrogen mustard ($HN_2$), so that the products of irradiation may be about three times as active as nitrogen mustard. Considering the nature of the calculations, the uncertainty of the mode of action of both types of agent, and the fact that local high concentrations of hydroxyl radicals are produced by radiation, it must be considered that the products produced by irradiation and nitrogen mustard have the same order of activity when compared on a molecular basis.

Although the radiomimetic cytotoxic agents may act by cross-linking within cells, there is some evidence that they have a different action. J. A. V. Butler and K. A. Smith (1950, [5]) have investigated the action of nitrogen mustard and other agents on thymonucleic acid. They have found that the active compounds produce a delayed depolymerization or breakdown of the nucleic acid molecule, similar to that found by Taylor, Greenstein, and Hollaender (1947, [16]) following X-irradiation. A similar breakdown of the nucleic acid, which can be followed by the fall in viscosity of the solution, occurs when free hydroxyl radicals are produced in the nucleic acid solution. The ratio of activity of the nitrogen mustard and X-rays in depolymerizing nucleic acid is about the same as in biological effects, i.e. $M \times 10^{-6}$ methyl *bis*-β-chloroethyl amine produces the same depolymerization as 100 r of irradiation.

These results suggest that the biological effects of radiation and nitrogen mustard may be produced by breaking down nucleic acid or other cellular constituents, rather than by cross-linking, although both mechanisms may play a part. The increased activity of the bifunctional compounds may be due to the fact that, after one group has reacted with a cell constituent, a free radical is formed by reaction of the second reactive group. If a free radical is produced within the tissue molecule, this may well decompose.

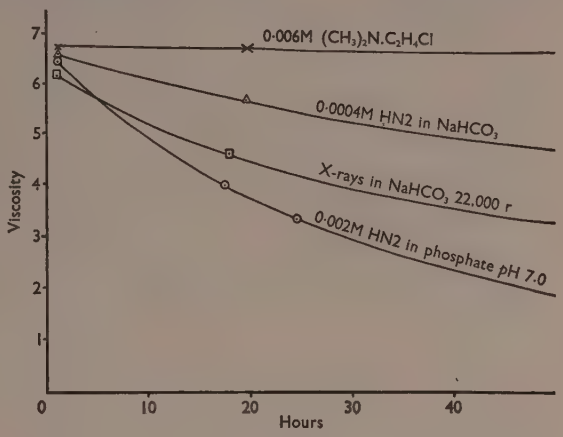



FIGURE 7 – *Curves showing the slow fall in viscosity which occurs in solutions of nucleic acid exposed to X-rays or nitrogen mustard. The fall in viscosity is due to breakdown of the structures of the nucleic acid molecule. (After J. A. V. Butler.)*

The fact that vesicants, carcinogenic hydrocarbons, and ionizing radiations should have similar actions may seem strange, but the effects are probably an expression of limited destructive power. If agents are very reactive chemically, or very destructive, they kill cells, and the specific biological changes described cannot be produced. Blisters, mutations, cancer, or chromosome-breaks can be produced only if sublethal toxic agents are applied. The radiation and radiomimetic effects are produced when specific agents of limited toxic action are applied to tissues, cells, or parts of cells, either by application of chemical substances, or by induction of chemical changes, such as the production of hydroxyl radicals, by radiations.

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# Natural rubber

L. R. G. TRELOAR

'The most remarkable quality of this gum, is its wonderful elasticity. In this consists the great difference between it, and all other substances. It can be extended to eight times its ordinary length, without breaking, when it will again resume its original form. There is probably no other inert substance, the properties of which excite in the human mind, when first called to examine it, an equal amount of curiosity, surprise, and admiration. Who can examine, and reflect upon this property of gum-elastic, without adoring the wisdom of the Creator?' —Charles Goodyear in *Gum-Elastic* (1855) [1]

## EARLY HISTORY

Familiarity tends to dull our curiosity; that which is commonplace is accepted as natural and inevitable. Yet most of us must have felt at some time something of the astonishment expressed by the American inventor Charles Goodyear when confronted with the properties of rubber. In addition to its elasticity, with which we are all familiar, rubber possesses a number of other less well known, though no less interesting, properties, which it is the purpose of this article to discuss.

First, however, a few words may be said about the development of rubber as an article of commerce, and as a subject for scientific investigation. Compared with most British major industries, the rubber industry is of relatively recent origin; it dates from the production of rubber-coated waterproof fabrics by Macintosh in 1823 at Glasgow and Manchester [2]. At about the same time Thomas Hancock (1786–1865) had invented a method of making rubber mechanically tractable, and later he became a partner in Macintosh's firm.

The applications of rubber grew steadily during the century, and by 1910 the production of wild rubber, mainly from Brazil, amounted to 80,000 tons per annum. The plantation industry, started in 1876 through the initiative of the British Government, with seedlings of the rubber-tree (*Hevea brasiliensis*) nurtured in the Royal Botanic Gardens, Kew, eventually surpassed and practically eliminated the native, and established itself as a basic factor in the economy of Malaya and the Netherlands East Indies rubber trade (figure 1). When the supply failed in 1942 we were saved from disaster only by the development of the American 'synthetic rubber' industry.

Though systematic research on rubber is a twentieth-century development, the material had been the subject of a number of isolated investigations during the previous century, and had attracted the attention of some of our ablest scientists. Outstanding among these earlier investigations is a paper by Faraday, delivered at the Royal Institution on 3rd February, 1826 [3]. According to the record [4], 'Mr Faraday explained the nature of caoutchouc (rubber), and gave the results of an analysis of the unchanged sap.' In this paper, Faraday showed that the rubber, which exists in the rubber-tree latex as fine particles in suspension, could be separated from the non-rubber constituents by successive dilution and creaming. The purified rubber was analysed chemically, and was shown to consist of two elements only—carbon and hydrogen, in the ratio 87·2 per cent. carbon and 12·8 per cent. hydrogen.

We now know that the pure rubber hydrocarbon has the chemical constitution $(C_5H_8)_n$, corresponding to 88·15 per cent. carbon and 11·85 per cent. hydrogen. Faraday's analysis was not the first to be published, but it was the most accurate at that time. That he should have succeeded, with the limited facilities then available, in arriving at a result so close to the true value, is evidence (if evidence were needed) of the minute attention to detail which permeated all his work.

More than a century was to elapse before a full understanding of the chemical constitution of rubber was achieved. We now know that the molecular weight is very high—much higher than was at one time thought possible—and that the molecule is built up of some 5000 units of the basic constituent isoprene ($C_5H_8$) and has an average molecular weight of 350,000 (figure 2). Even more remarkable is the fact that the isoprene units are connected end to end in the form of a single chain. The enormous length of this chain may be visualized by considering a model in which neighbouring carbon atoms are 5 in. apart; its total length would be approximately one

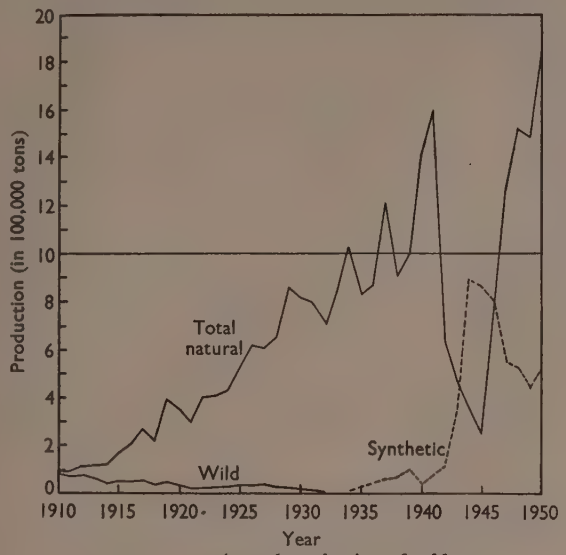


FIGURE 1 – *Annual production of rubber.*

mile. Staudinger, who was largely responsible for demonstrating the existence of long-chain structures of this kind, applied to them the now familiar term of macromolecules.

ELASTIC MOLECULES

The elasticity of rubber is very closely related to its long-chain molecular structure. This was first clearly realized by K. H. Meyer, who was struck by the similarity of its structure to that of a number of more or less highly elastic materials such as gelatin, collagen (the material of tendons), muscle protein, silk, and certain synthetic compounds. He saw that the normal thermal vibrations and rotations of the constituent atoms of a long-chain molecule must cause it to depart from the simple form of a straight rod, and to take up an irregularly kinked and continually fluctuating form. He saw, also, that in such conditions the molecule must exhibit elasticity, for if held in the fully extended state and then released, it will rapidly return to one of the statistically more probable kinked configurations.

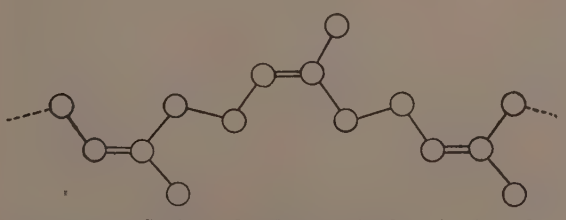

FIGURE 2 – *Section of rubber molecule, showing three isoprene units. (Hydrogen atoms omitted.)*

I have attempted to illustrate the form of a long-chain molecule as it would appear, for example, in a dilute solution, in figure 3, which is taken from a photograph of an actual model. This model represents the simplest type of long-chain structure, the paraffin or polyethylene molecule, $(CH_2)_n$, consisting of a chain of carbon atoms linked together by single bonds in such a way that the angle between successive bonds is $109\frac{1}{2}°$. The number of bonds in this model is 1000. If we imagine a molecule constructed in this way, but with twenty times the number of carbon atoms, we get some idea of the complexity of form of the average rubber chain.

Important conclusions can be drawn from the application of thermodynamics to Meyer's statistical or kinetic theory of elasticity. Two of them are of particular historical significance. It can be shown, first, that rubber should evolve heat in a

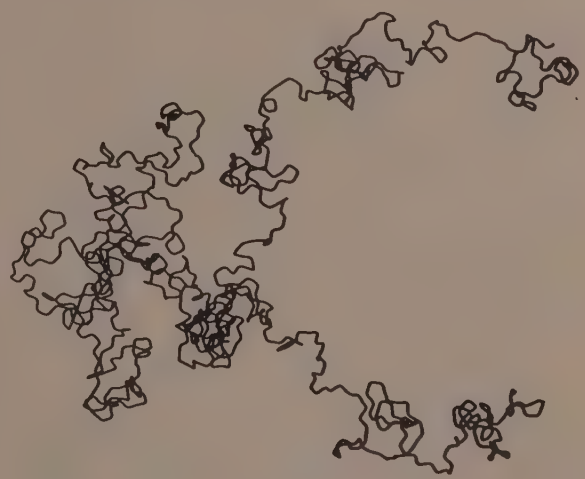

FIGURE 3 – *Model of polyethylene chain of* 1000 *links.*

reversible manner on extension, and, second, that the tension in a piece of stretched rubber should increase when the temperature is raised, or alternatively that the length should contract if the load is kept constant. These two effects were demonstrated by J. Gough in 1805, and confirmed by Joule in 1859. Figure 4 shows Joule's data for the heat of extension of vulcanized rubber, while figure 5 gives the relation between tension and temperature observed by Meyer and C. Ferri. The effects are quite large, and are easily demonstrated. Lord Kelvin, who co-operated with Joule, showed that the two effects are thermodynamically related, one being a consequence of the other.

Physically, the Gough-Joule effects have a simple interpretation. Since the elastic tension

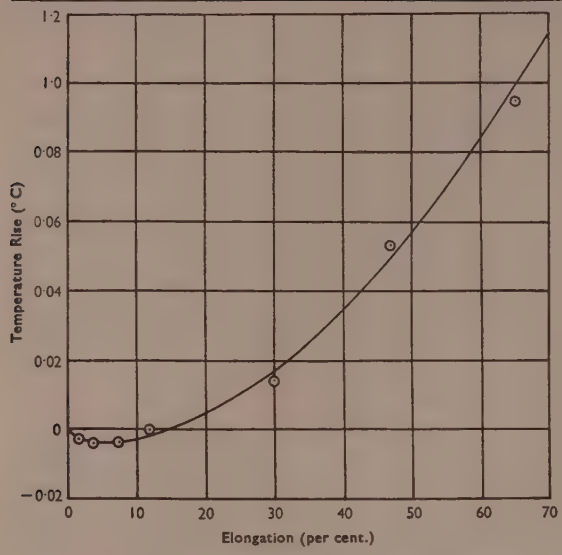


FIGURE 4 – *Temperature change on rapid extension of vulcanized rubber* (*Joule*, 1859).

originates in the thermal motion of the atoms of the molecular chains, an increase of temperature, which naturally increases the kinetic energy of the atoms, automatically increases the elastic tension. Moreover, when a piece of rubber is stretched at constant temperature, the average molecular kinetic energy (which is a function of the temperature only) is not affected. The work done on the rubber by the stretching force is therefore converted into heat. The two effects are strictly analogous to the phenomena exhibited by gases under the action of a compressive force. According to the well-known gas laws, the pressure at constant volume is proportional to the absolute temperature, and an increase of pressure (with reduction of volume) is accompanied by the evolution of heat. In both the rubber and the gas the elasticity arises from the same fundamental cause—random thermal motion.

### CHANGES OF STATE

From figure 5 it will be seen that the expected relationship between tension and temperature ceases to apply at low temperatures, i.e. below about — 60° C in the case of vulcanized rubber. This is because at these low temperatures the random thermal fluctuations which are the necessary basis for the elasticity can no longer take place, the kinetic energy being insufficient to overcome the electrical attractive forces between neighbouring chains. Under these conditions, the rubber loses its characteristic properties and be-

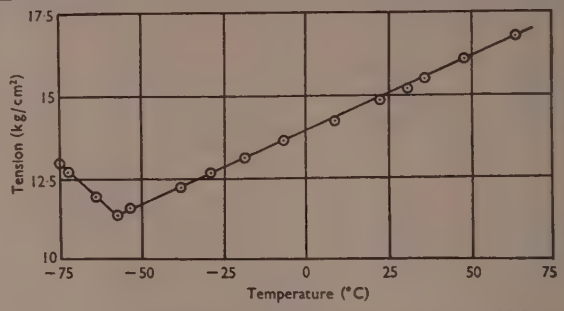


FIGURE 5 – *Dependence of tension on temperature.* (*Meyer and Ferri*, 1935.) *Vulcanized rubber*, 350 *per cent. extension.*

comes transformed to a hard, brittle, glass-like solid. This is easily shown by immersing a piece of rubber in liquid air, when it becomes rigid and brittle.

The phenomenon of the freezing-in of the instantaneous random-chain structure at low temperatures is not the only cause of the loss or modification of the normal elastic properties of rubber. Such a change can be brought about also by crystallization, which takes place when rubber is held for a sufficiently long time at temperatures in the neighbourhood of 0° C or lower. Crystallization is a slow process, and may take several weeks for completion; it leads to a considerable increase of hardness and loss of extensibility, but not to brittleness.

Crystallization involves the local rearrangement of neighbouring portions of long-chain molecules into a regular or lattice structure. The presence of crystallites is revealed by X-rays. Ordinary or amorphous rubber yields an X-ray diffraction pattern precisely similar to that of a liquid—one or more diffuse haloes or broad rings. Crystalline rubber, on the other hand, gives a pattern of sharp rings, like that of a crystalline powder, superposed on the amorphous or diffuse background. Such a pattern can have only one interpretation, viz. that the rubber contains crystallites, but that the state of crystallization is not complete. That is to say, the rubber is to be regarded as an intimate mixture of crystalline and amorphous components. This state is represented diagrammatically in figure 6(a). It is to be noted that any particular chain may pass successively through a number of crystalline and amorphous domains; this is because the molecules are much longer than the crystallites, and, being mutually entangled in a highly complicated manner, cannot separate out as individual entities.

On account of the continuous molecular connections between the crystalline and amorphous

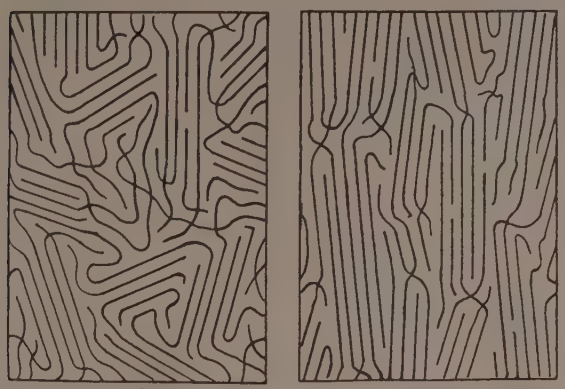


FIGURE 6 – *Representation of molecular structure of crystalline rubber:* (a) *unstretched,* (b) *stretched.*

components of rubber, the melting point of the crystallites is not precisely defined, but depends on the conditions of crystallization. The melting-point is always several degrees higher than the temperature at which the crystallization has been carried out. Hence it is possible for crystalline and amorphous rubber to coexist for an indefinite time.

### FIBROUS PROPERTIES

Rubber may be crystallized not only by freezing but by stretching. In the case of unvulcanized rubber particularly, the changes in physical properties brought about by such oriented crystallization are remarkable. The crystallites formed on extension are aligned in the direction of extension (figure 6(b)), and have the effect of maintaining the stretched state even in the absence of the stretching force. On raising the temperature, however, the crystals melt, and the rubber immediately retracts to its unstretched length.

Crystalline stretched rubber has the characteristic properties of a fibre, i.e. great strength in the direction of the fibre axis, with low strength in the transverse direction. This was discovered by Hock in 1924, who froze stretched raw rubber in liquid air and hammered it, whereupon it was found to split up into fibres, rather like a piece of wood. This effect was used by Hock as an argument in favour of his theory that rubber crystallizes on stretching—a theory which was finally confirmed by the direct X-ray evidence for crystallinity produced by Katz in the following year.

The close connection between crystallinity and fibrous properties is well shown by considering the accompanying table of tensile strengths for a number of materials.

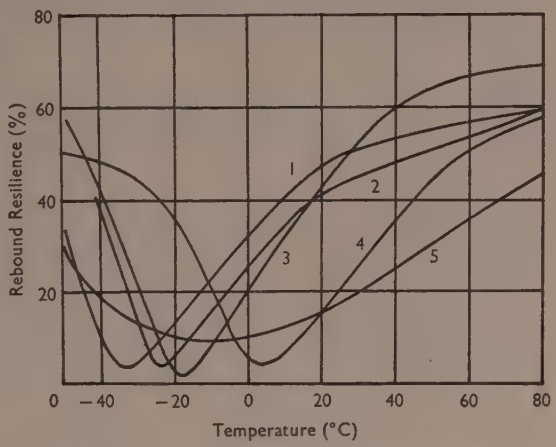


FIGURE 7 – *Rebound resilience of various rubbers as a function of temperature.* (*Mullins,* 1947.)
1. *Natural.* 2. *GR–S* (*butadiene-styrene*). 3. *Neoprene* (*polychloroprene*). 4. *Hycar OR* 15 (*butadiene acrylonitrile*). 5. *Butyl.*

The strongest fibres (flax, cotton, nylon) are known to be highly crystalline. Viscose rayon (regenerated cellulose) has, according to Hermans [5], a lower degree of crystallinity than natural cellulose. Natural rubber is actually stronger than glass, but GR–S rubber, which does not crystallize, is relatively very weak. It may, however, be strengthened by suitable treatment.

*Tensile strengths* (*calculated on cross-section at break*)

| *Material* | *Breaking strength* (*tons/sq in*) |
|---|---|
| Steel (piano wire) .. .. | 130 |
| Flax .. .. .. .. | 57 |
| Nylon .. .. .. .. | 44 |
| Cotton, silk .. .. .. | 38 |
| Rubber (natural) .. .. | 22 |
| Rayon (viscose) .. .. | 19 |
| Wool .. .. .. .. | 13 |
| Glass (sheet) .. .. .. | 13 |
| 'Synthetic rubber' (GR–S) .. | 2 |

### OPTICAL PROPERTIES

Rubber becomes doubly refracting when stretched, and the double refraction is enhanced when crystallization sets in. This double refraction may be demonstrated by stretching a thin sheet of rubber between crossed Polaroid plates; at small extensions the normal strain-birefringence is observed, but at an extension of about 250 per cent., when crystallization sets in, there is a

marked increase in birefringence. The differences between an amorphous polymer (e.g. polyvinyl chloride), a crystallizable polymer (e.g. natural rubber), and a fully crystalline polymer (e.g. polythene) when subjected to strain, are very striking.

### RESILIENCE

One of the most frequently encountered properties of rubber is its resilience, or ability to bounce. Not all 'rubbers' exhibit this quality to the same degree. Butyl rubber, for example, though reasonably elastic under slow rates of stressing, shows little elasticity or resilience under conditions of rapid deformation, such as occur when a ball strikes the ground (figure 7). On raising the temperature to 100° C, however, its resilience becomes comparable with that of natural rubber.

For all rubbers, lowering the temperature causes the resilience to fall to a very low value, but if the temperature is further reduced the resilience again increases. This phenomenon is associated with the changes in the configurations of the molecular chains which accompany the deformation. When the rate of readjustment of the chains is so reduced by the lowering of temperature that it becomes comparable with the time of deformation (i.e. of the order of a thousandth of a second) the response is poor, and loss of energy through internal viscosity results. However, if the temperature is so low that the rubber freezes to the glass-hard state, the molecular rearrangements cease altogether. The resilience is then due to a different type of elasticity, like that existing in a glass or crystal, and the characteristic high deformability of a rubberlike material is no longer operative.

### VULCANIZATION

In the early days of rubber manufacture the loss of elastic properties due to crystallization was found to be a serious disadvantage, particularly in cold climates. A still more serious disadvantage was the stickiness or fluidity which developed in warm weather. This was more apparent in the United States than in Britain, and at one time was so troublesome that it threatened to bring the whole industry into disrepute.

The softening of rubber at higher temperatures is due to two causes. Essentially, rubber may be regarded as a liquid of very high viscosity. The molecules are free to move with respect to one another, but, on account of the mutual entanglements of the very long chains, they alter their relative positions only very slowly. As the temperature is raised, however, the rate of molecular diffusion increases, and the viscosity is correspondingly decreased. This reduction of viscosity leads to loss of strength and to plastic deformation under stress, though it does not permanently alter the properties of the rubber.

The second cause of softening, and particularly of the characteristic stickiness of raw rubber, is oxidation, which increases with rising temperature, and is enhanced by exposure to light. Oxidation leads to the breaking of the long-chain molecules into shorter segments, and it is this effect which is so deleterious, since the viscosity of rubber diminishes very rapidly as the molecular length is reduced. Unlike the purely thermal softening, chemical degradation is an irreversible process, leading to permanent loss of elastic properties.

The great problem of eliminating this undesirable stickiness was eventually solved in 1839 by Goodyear, and independently by Hancock [6] in 1843, who invented the process known as vulcanization. Vulcanization consists in a combination of the rubber with sulphur, the sulphur atoms producing chemical cross-linkages between the chains, with the consequent formation of a continuous molecular network. The undesirable fluidity, which was dependent on intermolecular slipping, is thus completely suppressed. Rather unexpectedly, the tendency to crystallization is reduced as well, and, when crystallization does take place, its effects on the mechanical properties of the rubber are not nearly so serious.

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# The study of growth and form in plants

C. W. WARDLAW

The study of the origin of the morphological characters of plants may be claimed as one of the most ancient branches of biological science. Indeed, Aristotle and Theophrastus, in the fourth and third centuries B.C., may be regarded as pioneers in this field. It is now engaging the attention not only of morphologists but of workers on other subjects, and morphogenesis may well become a point of convergence of several branches of botanical science.

## MALPIGHI, WOLFF, AND GOETHE

The founders of plant anatomy, Malpighi and Grew, appreciated some of the problems of development. In his *Anatomia Plantarum* (1685), for example, Malpighi recognized the problems of seed development and leaf formation. It is, however, not until 1759 that we come upon unmistakable evidence of insight into the general problem of the genesis of form. In that year, Kaspar Friedrich Wolff, in his *Theoria Generationis*, announced his discovery of the apical growing point, or *punctum vegetationis*. Wolff was concerned with the general question of the origin and conformation of new parts. Was their development merely an enlargement and unfolding of organs already present—the so-called evolution theory: or was there a new construction of parts during growth—the theory of epigenesis? He was able to demonstrate that not all the leaf primordia of a bud were already present as rudiments, but that new primordia appeared successively at the upper extremity of the shoot axis—the growing point. Here, then, we see the inception of a general idea on the course of development, and an indication of the method by which new facts could be ascertained; but Wolff had no immediate followers, and the current of botanical investigation flowed in other directions and into different channels.

It is a curious fact that our next figure, Goethe, to whom we owe the word 'morphology,' was apparently not aware of the writings of Wolff. According to the most recent assessment (Arber, 1946), Goethe was an independent observer, a philosopher and man of letters who looked closely at plants, and who was imbued with the idea of developing some general conception, some nexus of ideas, to cover the diversity of form which he saw everywhere in Nature, as well as in every individual plant. His theory of metamorphosis (1790) does, of course, relate to morphogenesis, for it deals with 'the laws of transmutation according to which she [Nature] produces one part from another, and sets before us the most varied forms through modification of a single organ . . . the process by which one and the same organ presents itself to our eyes under protean forms, has been called the *Metamorphosis of Plants*.' A reading of his text shows that he was fascinated by changing forms, was interested in the underlying mechanisms (he referred to processes), and saw the need for achieving some kind of synthesis. The difficulty is that his general ideas on plant form prove, on close examination, to have an elusive quality. They do not, in fact, relate to any tangible process and therefore they have not provoked experimental work. On the contrary, his followers showed a strong tendency to stray along the easy and pleasant byways of poesy and nature philosophy.

## VON MOHL, NAEGELI, AND SCHLEIDEN

The contemporary phase may properly be said to have begun in the year 1842, when Schleiden published his book *Grundzüge der Botanik* ('Outlines of Botany'). The followers of Goethe made little progress in the investigation of plant form and structure: too many of them were imbued with an authoritarian and scholastic outlook, and with the notions of idealistic morphology. There were of course other attractions, and much fine work was done in systematic botany. Alphonse de Candolle has given the following impression of biology in the early years of the nineteenth century: 'After the great wars of the beginning of the century, collections were suddenly enlarged through the many and distant travels of capable naturalists. An infinity of specimens, animal and vegetable, so brought home from all parts of the earth, called imperatively for description, naming, and classification. Science was, so to speak, swamped; and in studying even the most apparent among the forms presented, there was material enough to tire out a whole generation. This work was actually in progress when better microscopes were invented and ways of using them brought to perfection.

The range of objects for study was enlarged in this and that direction; and such research became the favourite occupation of nearly half the naturalists.'

What really opened up the new, and more scientific, phase in botany was the incidence of a number of brilliant investigators. Hugo von Mohl observed cell division; he gave us the word 'protoplasm,' as well as some of the leading ideas that go with it; he indicated the cell as the unit of construction in the plant body; and, in short, he restored the study of plant anatomy. Then, in 1842, Schleiden published his celebrated treatise, described by Goebel as one of the most remarkable and characteristic books that have ever appeared in botany. The author trenchantly preached a new gospel: that the highroad to discovery lay in the study of development, and that this knowledge is the foundation of all insight into morphology. It was not so much that Schleiden's own botanical work was of a higher order—indeed, he made many mistakes—but he had very clear ideas on where the real problems lay, and very strong ideas on the misdirected activities of his elders and contemporaries. He saw the faults of botanical science, and pitilessly denounced them and their authors. These criticisms proved exceedingly refreshing and stimulating, at least to the younger generation of botanists, on whom indeed they made a profound impression. The key to morphology, he reiterated, lies in the study of development, and the key to physiology in the study of the living cell. How pertinent these views are to morphogenesis, and how very modern they sound! In trying to explain or interpret what we see in living organisms, as he said in 1838, 'we do but grope about in the dark if we do not apprehend it as a Thing Becoming, ever changing, and if we judge it only in its developed stage.'

Naegeli, too, was at work, and in the years 1844–6 addressed himself to the questions of how cells are formed in the growing vegetative organs, and how far the processes are the same in the lower cryptogams and in the vascular plants. He discovered the apical cell, that characteristic feature in the organization of many plants, and, together with von Mohl, he founded and elaborated the theory of cell formation. This was a momentous discovery, for it directed attention to the importance of apical growing points as the fundamental formative regions in plants—a view that prevails today when students of morphogenesis are concentrating on the shoot apex as the primary morphogenetic region. Naegeli's conception of development is given in Sachs' *Geschichte der Botanik* ('History of Botany') as follows: 'Since in Nature everything is in movement and every phenomenon is transitory, presenting itself to us in organic life especially as the history of development, all due regard must be paid to their condition of constant mobility in forming scientific conceptions. The history of development is not merely to be treated generally as one of various means of investigation, but as identical with investigation into organic nature.'

The lower cryptogams (non-vascular plants) were the chief subjects of Naegeli's initial investigations of apices, but later his work was extended to the higher cryptogams (the ferns and their allies) and phanerogams (seed plants), i.e. he proceeded from a study of the simpler to the more complex and difficult types of organization. Closely connected with this methodological innovation, he made the new doctrine of the cell the starting point of morphology, i.e. the initial development of organs and their subsequent growth were both related to the formation of the separate cells. He showed that in many of the cryptogams every organ has a single cell at its apex, and that all the succeeding cells which constitute the tissue are formed by the division of this one cell according to fixed laws. These observations, amplified by Hofmeister and others, have served as a basis for many developments in botanical science. To Naegeli, Sachs has paid the tribute that his was the first attempt 'to apply mechanico-physical considerations to the explanation of the phenomenon of organic life,' i.e. he referred the growth and inner structure of organized bodies to chemical and physical processes.

One important result of the work of Naegeli and his followers was that a vast amount of detailed information on the structure of the growing regions of plants was brought to light, and thus materials especially favourable for investigation of morphogenesis became generally known.

### HOFMEISTER AND SACHS

We now come to what may well be described as a luminous period in the history of morphogenesis. In 1851, Hofmeister published his *Vergleichende Untersuchungen*, later to appear, with additional papers, in an English translation under the title of 'Higher Cryptogamia' (1862). Such a work has its place in this history, for all studies of morphogenesis necessarily rest on a basis of morphological observations, particularly those which illustrate

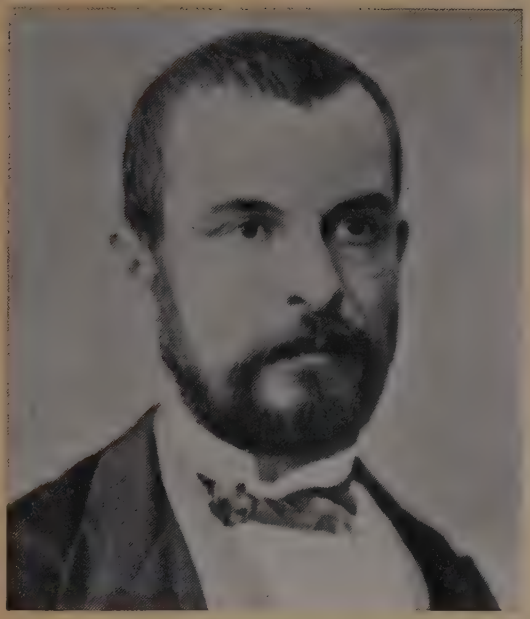

FIGURE 1 – *Wilhelm Hofmeister* (1824–77).

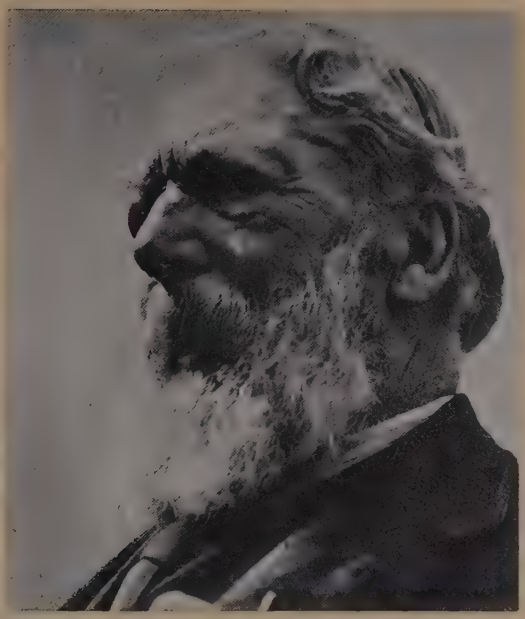

FIGURE 2 – *Sir D'Arcy Wentworth Thompson* (1860–1948).

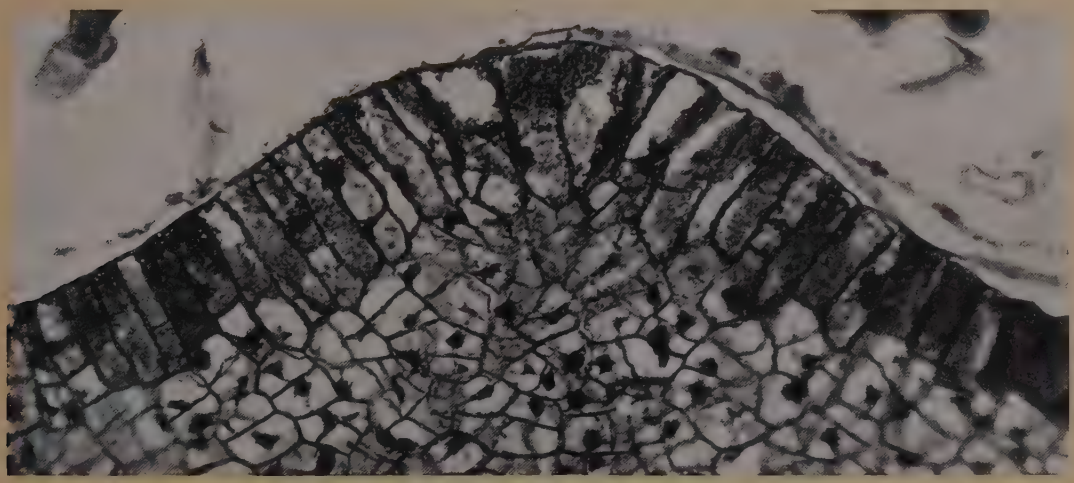

FIGURE 3 – *Apex of* Dryopteris.

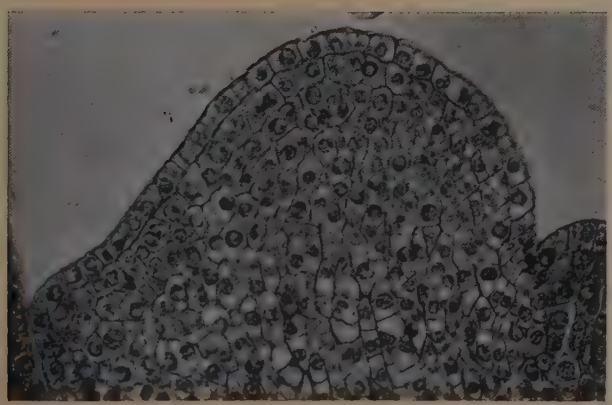

FIGURE 4 – *Apex of* Phaseolus.

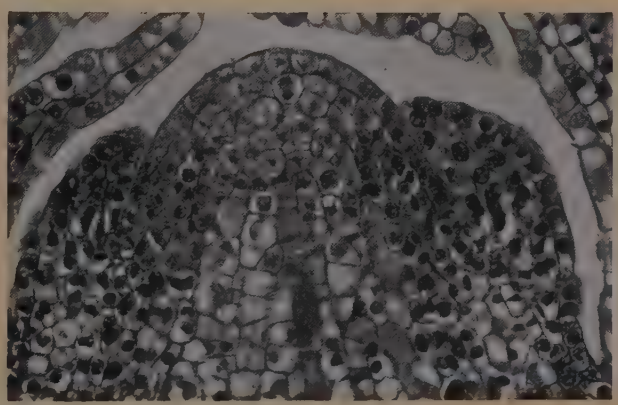

FIGURE 5 – *Apex of* Taxus.

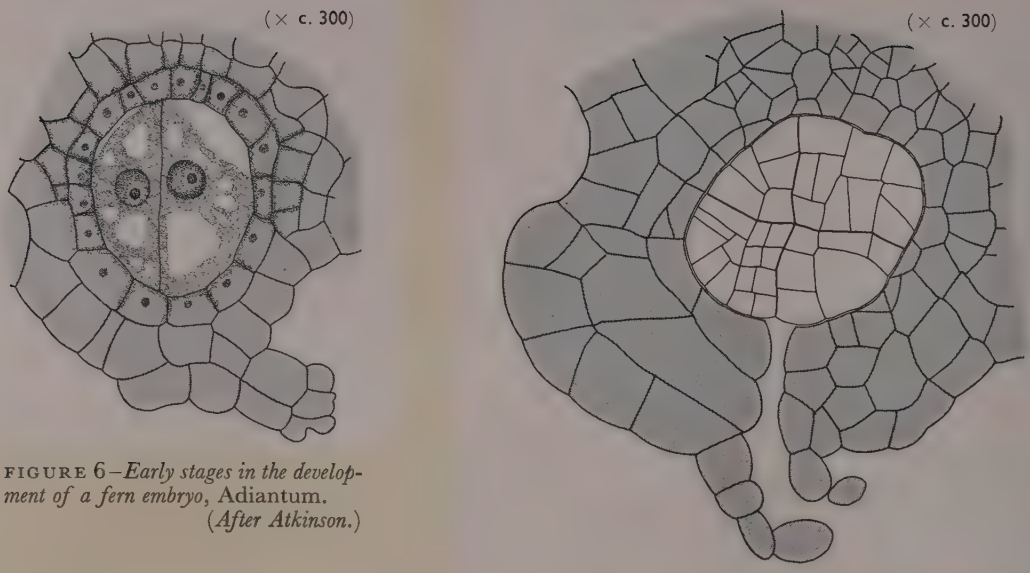


FIGURE 6 – *Early stages in the development of a fern embryo*, Adiantum. (*After Atkinson.*)

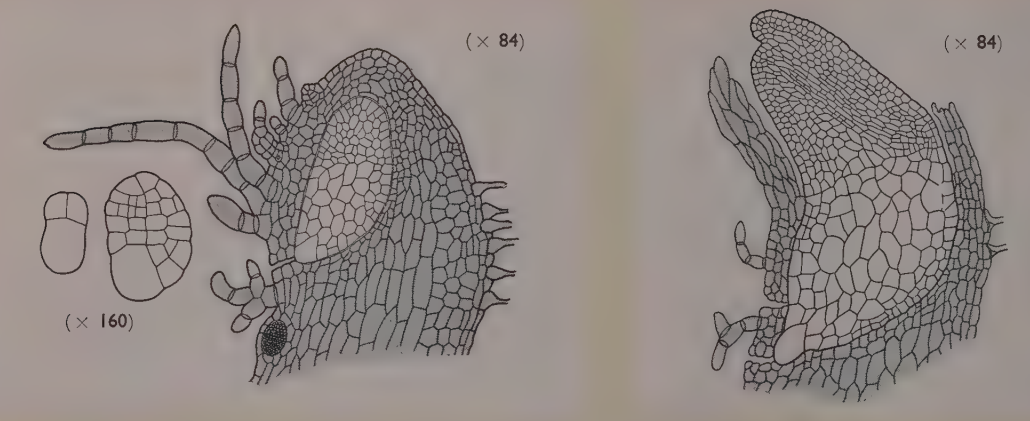


FIGURE 7 – *Stages in the development of the embryo in a lycopod*, Lycopodium selago. (*After Bruchmann.*)

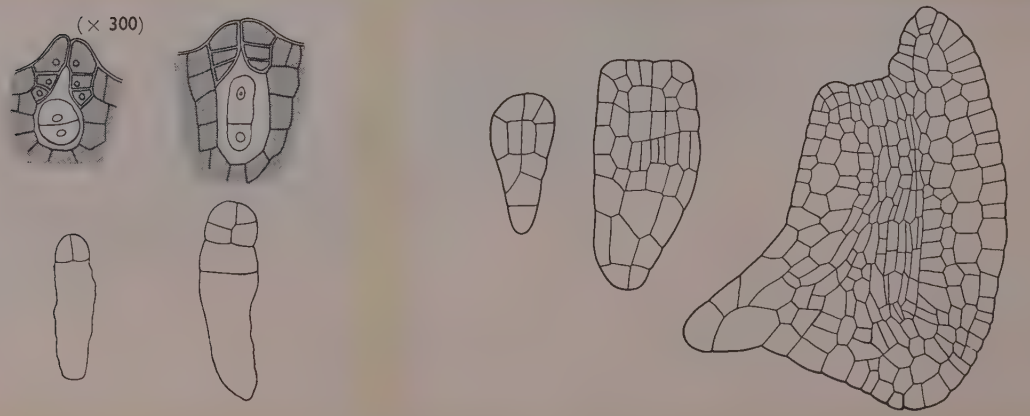


FIGURE 8 – *Stages in the embryonic development of* Selaginella spinulosa. (*After Bruchmann.*)

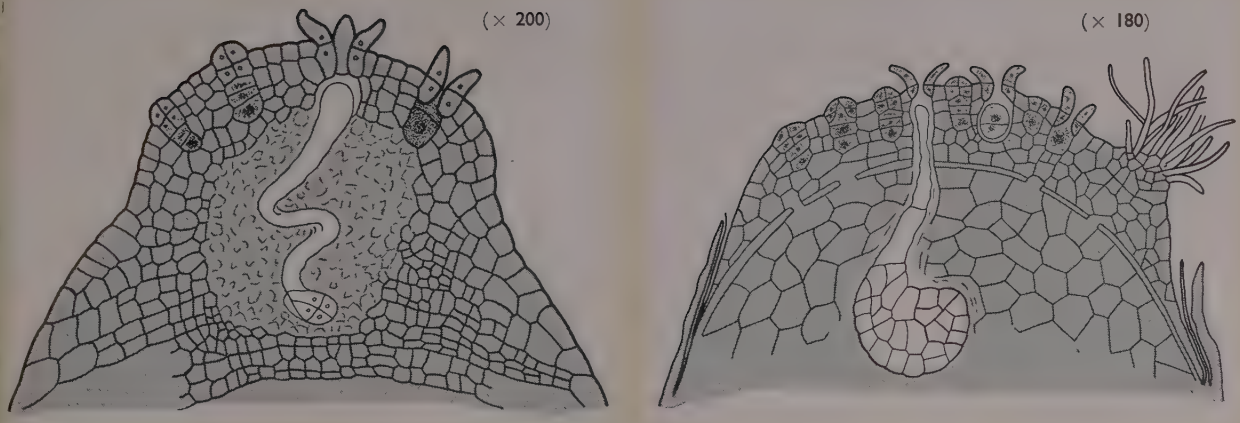


FIGURE 9 – *Early stages in the embryogeny of* Selaginella galeottei *and* S. poulteri. (*After Bruchmann.*)

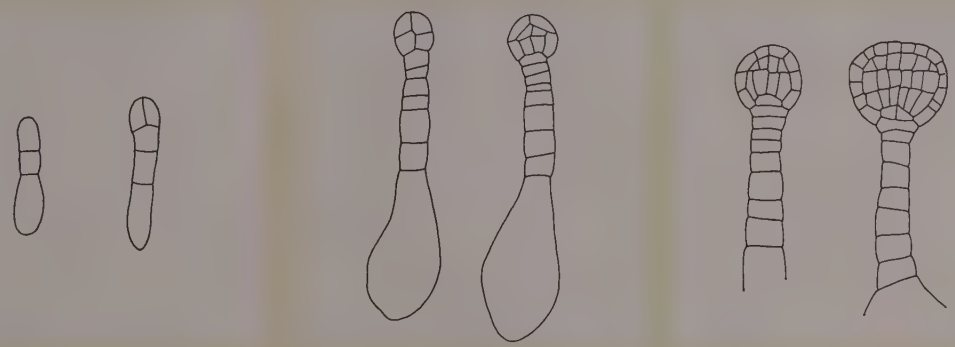

FIGURE 10 – *Early stages in the embryogeny of a flowering plant, shepherd's purse,* Capsella bursa-pastoris. (*After Souèges.*)

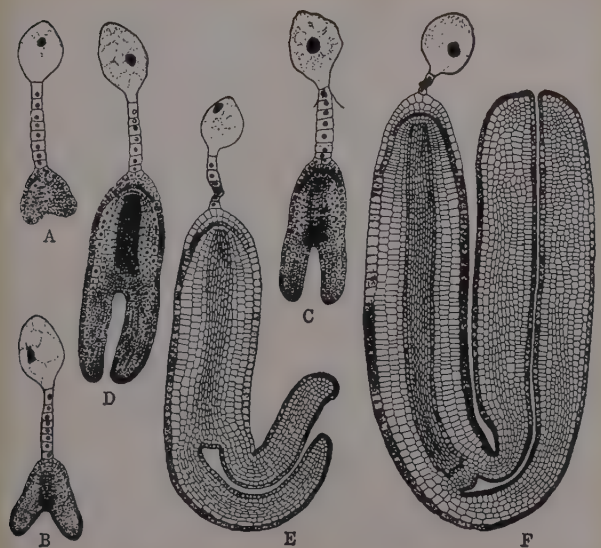


FIGURE 11 – *Later stages in the embryogeny of* Capsella. (*After Schaffer, by permission from 'An Introduction to the Embryology of Angiosperms' by P. Maheshwari; copyright* 1950, *McGraw-Hill Book Company Inc.*)

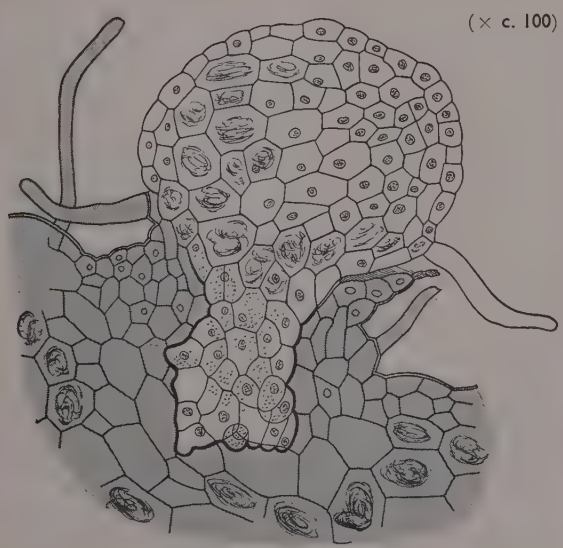


FIGURE 12 – *Embryo of a leafless, rootless pteridophyte,* Tmesipteris. (*After Holloway.*)

the consecutive stages in the development of individual organisms. Now, as even the most cursory study of the 'Higher Cryptogamia' will show, Hofmeister, by means of accurate drawings and descriptions, was able to give a vast amount of new information on the development of the gametophytes and sporophytes of bryophytes, pteridophytes, and seed plants. These studies are perhaps best known as marking the beginnings of our insight into the alternation of generations. That was undoubtedly a very important contribution. It is not less important that he provided a great deal of essential information on the progressive morphological and structural changes during the individual development. These descriptive studies had a still further importance: they prepared the way for his subsequent study of the factors underlying the observed developments.

Another important descriptive and illustrated work, in which floral organogenesis is treated in considerable detail, appeared contemporaneously. This was Payer's *Organogénie de la Fleur* (Paris, 1852).

As Hofmeister's work progressed, it ceased to be merely descriptive. It was not enough for him to observe that during the development of a particular species a regular succession of characteristic changes in form and structure took place. He constantly inquired how the observed form came to be; to what processes of growth the observed structural developments could be related; and what internal and external factors determined specific structural organization. The substance of such investigations he described in 1868 in his *Allgemeine Morphologie der Gewächse* ('General Morphology of Plants'). In this work, he tried to introduce mechanico-physical ideas into his morphological studies, and to derive generalizations from them and from the data of physiological experiments.

Hofmeister's approach to the problems of causal morphology was not only refreshingly new and direct, as compared with the contemporary writings of the nature philosophers and idealistic morphologists: it also had the qualities of range and diversity. Thus his contributions included a general statement of the problem, with growth in the centre of the picture; studies of the inception of axes and their appendages, i.e. of the formative activities at the shoot apex; leaf formation and phyllotaxis (of which he originated the mechanistic interpretation); the effect of external factors, e.g. light and gravity, on plant conformation; the conformation of embryos in seeds; the effect of invading organisms, e.g. the study of gall-formation, as a means of investigating causal factors; the mutual effects of adjacent organs; the effect of environment, as in water plants; and the factors determining the position of the partition walls in dividing cells.

In his book *Die Lehre von der Pflanzenzelle* ('The Doctrine of the Plant Cell'), Hofmeister in 1867 made the important generalization that it is the organism as a whole that is the unit of construction, not the individual component cells. In all this work, form-relations are presented as conditioned by growth, and an attempt is made to investigate the relevant phenomena. It is important, and no more than justice, to recognize how very modern Hofmeister was in his general outlook on morphogenesis. It is a fact that his work considerably preceded the developmental mechanics (*Entwicklungsmechanik*) of the zoologists. Thus, in considering factors in morphogenesis, he emphasized that the 'specific, hereditary, unknown forces' are those which are of primary importance. With them, act the better-known external forces, such as gravity. 'And this cooperation gives a result of mixed nature: a conformation which enables us to recognize the influence of the second force (i.e. extrinsic factors) as decisive in minor features. Most evident of all is the way in which the form of the plant is influenced by a force or a sum of forces acting in a vertical direction.' (*Allgemeine Morphologie.*)

While comparative morphology was sweeping on its way in the interests of phylogeny (as we shall see later), and becoming a progressively more restricted discipline—witness the writings of botanists in the last decade of the nineteenth century—some botanists nevertheless did continue to follow in the steps of Hofmeister. Chief among them was Sachs, who was not only a leading exponent of plant physiology, but a morphologist whose writings were imbued with the keenest interest in the problems of causality. His book *Vorlesungen über Pflanzenphysiologie* (1882; English translation, 'Lectures on the Physiology of Plants', 1887), a work that exercised a profound influence on British botany, contains many examples in which the development of form is referred to physical factors and mathematical relationships. In 1877, he formulated his rule of rectangular section, i.e. that in all tissues new cell walls are laid down at right angles to those already present: this was, in fact, an extension of Schwendener's hypothesis of 1860. In this interest in the inception of tissue pattern he had two important contemporaries, Berthold and Errera, who in 1886

independently put forward physical explanations of the position occupied by the partition wall when a cell divides; in other words, they laid the foundations for a scientific account of the development of cellular pattern, or histogenesis. They proposed the hypothesis that when cells divide they do so by walls of minimal area, the physical factor involved being surface tension. The value of this and related conceptions is at once apparent when we consider how similar are the segmentation patterns in the embryogeny of a wide range of plants, or at the apices of algae, bryophytes, and pteridophytes.

Sachs has a yet further claim on our attention. He propounded the theory of chemical correlation which has reached its heyday in contemporary botanical and biochemical studies. Growth and morphogenesis are inseparable: the analysis of a morphogenetic process is an analysis of growth and therefore of metabolism, and, in particular, of specific metabolites. In Sachs' ideas, therefore, we see a beginning that has led to the numerous contemporary works on plant biochemistry, phytohormones, and related subjects.

### A NEW DEPARTURE

It might be thought that, as a result of Hofmeister's investigations and his critical search for the relationship between physiological activity and the assumption of form, botanical science had at length been established on a broad and sure foundation—one in which morphology and physiology were accepted as inseparable aspects of the same theme. A period of rapid progress might be expected to have followed. As a matter of fact, it did not. Perhaps botanists were not quite ready for Hofmeister's new outlook. The subject and the problems proposed were of extreme difficulty, and the master's writings, which were condensed and somewhat abstruse, were not always easy to comprehend. But there was another and very understandable reason. Darwin had just published his *Origin of Species* (1859). In what has been called the phyletic period—that which followed the publication of the theory of descent—the details of plant embryogeny and of the form and structure of the adult, together with such facts as could be culled from the fossil record, were regarded chiefly as providing materials for comparative studies, and for the construction of phylogenetic systems. Darwin's views had a sweeping success. The mechanistic problems of general or causal morphology were left on one side: comparative morphology had come into its own, and was soon regarded as a distinct and separate discipline. One inevitable result was the formulation of concepts of a purely morphological character. Some of these, being divorced from physiology, were likewise more than a little divorced from reality. Botanists were no longer preoccupied with the question: How does the observed form come to be, in terms of physical, physiological, and other factors? They asked rather: What family relationship is indicated by the observed form or structure, and what light does this information throw on the course of evolution? The relation between form and function, which Sachs and, later, Goebel described as organography, was, of course, of importance to those who maintained the Darwinian position and assumed the all-pervasiveness of adaptation in plant life. On the other hand, the factors relating to the formation of organs and the differentiation of tissue systems for the most part remained unexplored. Several decades were to pass before the methods or conclusions of the phyletic morphologists were seriously challenged.

### THE REVIVAL OF CAUSAL MORPHOLOGY

The literature of the 1890's shows how confident the comparative morphologists were that their branch of botanical science was a self-contained, independent subject, with which physiology had nothing to do. By the second decade of the twentieth century a change had set in. Botanists were beginning to have doubts about the merits of comparative morphology as a separate discipline; they had also reason to doubt some of its major conclusions. It began to appear that the monophyletic tree of the plant kingdom, as conceived by the more enthusiastic followers of Darwin, such as Haeckel, in which algae, mosses, ferns, gymnosperms, and angiosperms all stemmed from a single trunk, was not in keeping with the facts as revealed by widening experience. In particular, the evidence that parallel evolution, or, as Ray Lankester described it, homoplastic development, was widespread in the plant kingdom, that comparable major morphological innovations and developments had occurred in groups that were in no way related, all indicated that the conception of a monophyletic tree must be replaced by a construction in which parallel evolution was given due weight. Once the critics had firmly grasped this fact, comparative morphology rapidly lost ground.

Our historical survey thus brings us to the British Association meeting of 1915, when Lang, in his presidential address, dealt with the theme

of 'Causal and Phyletic Morphology.' In this noteworthy paper, he showed clearly the relative positions of the two aspects, indicated the parlous condition of morphology when pursued purely as a comparative study, and pointed to the wonderful opportunities afforded by inquiries into causality. Even if the phyletic history of plants were before us in full, he said, the problems of causal or general morphology would still await solution. As to the parallel developments which had proved such a stumbling block to the phylogenists, Lang took quite a different view: the fact that there are so many instances of homoplastic development—or homologies of organization as Sachs and Goebel had described them—makes it all the more important that they should be studied with particular reference to the factors responsible for bringing them about. So, once again, the emphasis is on the factors involved in the inception and development of form and structure. In particular, the need for experimental and physiological studies of morphogenetic processes at the shoot apex was indicated. A few years later (1923), in another presidential address to the British Association, Sir Arthur Tansley reiterated these views. Comparative morphology was ceasing to attract the younger botanist; the future of botany lay in the study of the process of development both in the individual and in the race; and the task was to determine the forces which lay behind these developments.

### FROM 1910 TO 1930

This period thus stands out as one of special importance, not so much in terms of achievement in the study of morphogenesis in plants as in the ferment of ideas relating to new experimental work. In 1917 there appeared a remarkable book by Sir D'Arcy Thompson, called 'On Growth and Form.' This is *par excellence* a work on morphogenesis, and one which has exercised a stimulating influence on a widening circle of investigators. To D'Arcy Thompson, living organisms were just as full of mystery and of unknown elements as they were to many a vitalist. But he seized upon one important idea, and firmly held to it: in plants and animals we are, after all, dealing with matter; the organs of plants are so many portions of matter; and the particles which compose these organs must be moved and conformed according to the laws of physics and mathematics. 'In general (he says) no organic forms exist, save such as are in conformity with physical and mathematical laws.' That is the main thesis; and with illuminating examples drawn from both the plant and the animal kingdoms, and a supreme elegance of handling, he showed how many of the forms and structures that are of special interest to morphologists, and especially to students of morphogenesis, can be explained by reference to comparatively simple physical laws and mathematical relationships. That, of course, is not quite the same thing as proving that the observed structures are due to the physical factors or spatial or mathematical relationship to which D'Arcy Thompson refers them; indeed, some sections of the book have been severely criticized.

About the same time, another important work on morphogenesis appeared. This was a small book by Child, 'Individuality in Organisms' (1915), in which he set out the thesis that physiological gradients in plants and animals have been potent factors in determining their morphological development. Over the years, Child and his pupils have collected information on this aspect of morphogenesis, a comprehensive statement appearing in 1941 under the title 'Patterns and Problems of Development.' A more purely botanical exposition along the same general lines has been given by Prat (1945).

During this period, also, we see the ferment of ideas affecting botanists the greater part of whose work had been in the comparative field. Thus, Bower, in whose earlier writings the stele (or vascular system) in pteridophytes had been regarded as affording one of the most substantial of the criteria of comparison because of its assumed conservative nature, in 1921 wrote his well-known paper 'Size a Neglected Factor in Stelar Morphology,' and in 1930 his book 'Size and Form in Plants.' With illustrations drawn from a wide range of pteridophytes, he showed that increase in stelar complexity goes hand in hand with an increase in size, and that a fuller understanding of this phenomenon, which we now describe as the size-structure correlation, must be sought in those regions where it is established, that is, in the apical growing point. In 1922, still bent on opening up new inquiries into causality, Bower had dealt with the embryogeny of plants and showed how, over the whole of the plant kingdom, the polarity of the organism is determined at the first division of the zygote, and how very general indeed is axiate development—one of those remarkable homologies of organization to which Lang had referred. An important feature of this study was the attempt to find experimental

evidence relating to morphogenetic processes in the developing embryo.

At this point it is perhaps relevant to say a few words about Goebel, though it is particularly difficult to know how, or when, to treat the work of this eminent botanist. His great book, *Organographie der Pflanzen* ('Organography of Plants'), was first published in 1897, and has run to an English translation (1900), and to two further German editions, published in 1913 and 1928. In this book, in which there is naturally some change in point of view over the years, there is an amazing accumulation of observation on the growth and development of plants, informed as opportunity offered by the results of experimental investigations. Goebel's studies, collectively described as organography, were primarily concerned with the configuration of plants as affected by factors in the environment. 'Morphology has to determine in what degree the formation of organs shows an adaptation to external relationships, and to what extent it is dependent upon these and upon internal conditions.' That his views included those which we should today regard as being appropriate in a student of morphogenesis is clearly indicated by such statements as that 'to recognize the factors which bring about the development of say a leaf with one side larger than the other is infinitely more important than to construct a phylogenetic hypothesis unsupported by facts.' By organography, in his earlier writings, he means the reciprocal relation of form to function, with environmental factors taking a leading place, whereas, as he makes clear in his *Einleitung in die Experimentelle Morphologie* (1908), the study of organogenesis is primarily concerned with developmental history in the individual organism. Goebel's books and numerous scientific papers constitute a mine in which the contemporary student of morphogenesis will almost certainly find a great deal that is relevant to his own particular investigations; he will also encounter illuminating ideas, and a considerable amount of experimental work, on morphogenesis.

### THE CONTEMPORARY OUTLOOK

The contemporary period—which (somewhat arbitrarily) may be held to comprise the last two decades—has been characterized by some notable advances, and a great increase of interest, in the study of morphogenesis. Not least important is the beginning of a real confluence of the several streams of knowledge into one main channel of approach to the problems of morphogenesis, which should culminate in an embracing conception of the organization manifest in all plants.

During this period there have been extensive anatomical investigations of apical meristems and organ formation in all classes of plants, and experimental studies of bud, root, leaf, and flower formation, phyllotaxis, and tissue differentiation, by the use of surgical techniques, the methods of tissue culture, and the control of environmental factors. Investigations of growth, and in particular of the physiology, biochemistry, and morphogenetic activity of growth-regulating substances, have been undertaken in attempts to establish the relationship between biochemical activity and the assumption of form. This period, too, has seen the inception of a new and fundamental branch of biology, namely physiological genetics. Thus recent textbooks of genetics typically contain a chapter on morphogenesis. There must indeed be few contemporary botanists who would deny that genetical factors—the genes, in their several kinds and combinations—are at work in each and every phase and aspect of the morphogenetic process. Cytogenetics and enzymology now tend to advance in very close conjunction, and little by little are being brought into relation with the physiology of growth and the facts of development as ascertained by the morphologist. The hereditary particles, the genes, are large organic molecules, or aggregations thereof, arranged in a particular way in the chromosomes, and their primary action in the plant cell is biochemical; in fact, they determine the specific metabolism of the organism. In the correlative structural developments, both the biochemical and biophysical properties of the matter of the living cell are involved. Electron microscope, X-ray, and other recent techniques have begun to make possible the exploration of the submicroscopic structure of living materials. It is unnecessary to elaborate further: the numerous symposia on different aspects of morphogenesis during recent years bear witness to the importance of this theme in contemporary botanical science.

The materials for the study of morphogenesis are the embryonic and growing regions of plants. Thus the successive stages in the development of the fertilized ovum in vascular plants afford remarkable examples of the establishment of axiate development, cellular pattern, and the inception of shoot, leaf, and root. Some of these are illustrated here. In each instance, the task is to explain the factors—both intrinsic and extrinsic

—which are at work in producing the observed structure, the progressive elaboration of form, and the completed unity of the individual. In practice, the embryos of vascular plants have proved difficult subjects for experimental investigations, though some interesting work is now beginning to appear, and more may be expected as new techniques are devised. Students of morphogenesis have accordingly had recourse to a more accessible region, the perennially embryonic shoot apex. Since the apices in different classes of vascular plants show great histological diversity (figures 3–5), some having a conspicuous apical cell in the most distal position, others having a characteristic zoned or layered construction, the several types of apex carry their own interest and pose their own special problems. In recent years, a large amount of new research has been done on the shoot apex by direct anatomical methods, and experimentally by using surgical techniques, the methods of tissue culture, and biochemical analysis. The comparison of apices in materials of known genetical constitution is also proving a fruitful field. With the onset of flowering, the vegetative apex undergoes a remarkable transformation: it becomes the seat of formation of the several floral parts, and a new series of problems in morphogenesis confronts the student. Indeed, in the development of any plant, during which its characteristic organization becomes manifest, there are problems of morphogenesis, the solution of which may well require contributions from all branches of the general corpus of botanical knowledge.

### THE FUTURE

The orthodox historian, as a rule, is content to leave the future to take care of itself, but, as we have only recently crossed the threshold of a new half-century, it may perhaps be permissible to look forwards as well as backwards. The outlook for botanical science may justly be regarded with some optimism, for never has there been a period so varied and stimulating, so fraught with interest and exciting possibilities and opportunities, as the present time and that which lies immediately ahead. Can we but rise to a level of scholarship that does justice to this abundant period of discovery, and effect some integration of the different branches of the science, the golden age of botany may well be at hand. Morphogenesis, as much as any other contemporary theme, would seem to provide a suitable focal point.

# Book reviews

### BRITISH WILD ORCHIDS

**Wild Orchids of Britain**, *by V. S. Summerhayes.* Pp. xviii + 366, *with numerous coloured plates, monochrome half-tone plates, and line drawings.* *Collins, London.* 1951. 21s. *net.*

This is another attractive volume in an excellent series. Never before has a book appeared which gives a full, up-to-date, and readable (yet scientific) account of the British orchids, fully illustrated in colour and at an attainable price; Col. M. J. Godfery's monograph, which appeared in 1933, was expensive, and few copies were printed. The book begins with a general account of the fantastic life-history of orchid plants, and of their extraordinary interrelation with saprophytic fungi. There follow chapters on the structure of the orchid flower, on pollination and fertilization, on geographical and ecological distribution, and on classification. The largest section of the book is occupied by chapters dealing with the genera singly or in groups, and the account is completed by a key for the determination of the species, a glossary, a bibliography, and a series of maps showing the distribution in the British Isles of the individual species. The coloured plates, prepared from colour photographs, make an attractive feature, and do not suffer so much from variations in quality as do the plates in some volumes in this series. They are not first-rate, but perhaps this cannot be expected at the price at which the book is published. The text is thoroughly interesting, and is evidently informed by wide first-hand knowledge on the part of the author. It contains minor blemishes, in the form of small mistakes or of statements needing revision, but these are not of a serious nature.

T. A. STEPHENSON

### BRITISH SCIENTISTS

**British Scientists**, *by E. J. Holmyard.* *Pp. viii + 88. With 24 portraits.* *J. M. Dent and Sons Limited, London.* 1951. 6s. *net.*

'British Scientists' tells the story of Britain's contribution to the advancement of science. This small and attractive volume is sure of a warm welcome, for biographies of eminent men of science have caught the public's fancy.

There are two dominant schools of historical thought—one which views history in the light of its heroes, and another seeing history as a progression of ideas. Ideas, however, do not progress alone. They need men to express and propagate them. Dr Holmyard gives an account of some of the British scientists who have been in the van of scientific progress, and in addition he writes about British scientific societies and institutions which have played so great a part in the development of scientific knowledge. The selection of material could not be improved. Early chapters tell of Gilbert's great work on the magnet, Napier's invention of logarithms, Harvey's discovery of the circulation of the blood, and Newton's *Principia*. Closer to our own time, accounts are given of Lister, Kelvin, Ramsay, and Rutherford. Britain may well be proud of the long succession of

eminent men of science portrayed in this volume. 'British Scientists' will appeal to all readers of scientific literature, not only for the wealth of information it carries, but because it is written in a scholarly style which is always captivating and never dull. Further, Dr Holmyard has resisted the temptation to dramatize his subject. The twenty-four portraits are an attractive feature of the book.

W. WARDLAW

EXPERIMENTAL PSYCHOLOGY

Handbook of Experimental Psychology. *Edited by S. S. Stevens. Pp. xx + 1436. John Wiley and Sons Inc., New York; Chapman and Hall Limited, London. 1951. 120s.*

A comprehensive textbook may be one of the easiest or one of the hardest kinds of publication to review. The easy way is to make a list of the main section headings and of the contributors, and to the reader who is already well instructed this may be extremely enlightening. The hard way is to attempt an appraisal of the value of the contribution that is made to the systematic presentation of knowledge, or perhaps even to scientific advance.

In this case the publishers have already done the first. 'Thirty-four leading scientists,' they say, 'contribute nearly one million words to this definitive account of Neurophysiology . . . Homeostasis . . . Endocrine function . . . Measurement . . . Psycho-physics . . . Sensory functions . . . Learning . . . Motivation . . . Perception . . . Selection . . . Training . . . Applied experimental psychology.'

Opinions may vary as to whether there is any particular virtue in a million words, and also as to whether a handbook of experimental psychology need have been quite as heavily weighted as this one in the direction of straight physiology. But these, and all considerations of what should be left out and what should be put in, are the proper concern of the editor and his advisers. They have stated their aims clearly: that they would not try to include everything that could be called experimental and psychological, that they would allow their contributors a large degree of freedom, that they would appeal to the advanced student and to the specialist; and that they would provide these readers with a guide and a reference source to topics related to their own particular specialized fields. These are reasonable and sensible aims, and, accepting them, no reader is likely to be disappointed. Naturally, it is not a book to be perused straight through. So far as I am concerned, I have picked out what I think to be a representative sample of the topics, and I have been deeply impressed by the accuracy of the learning, the high quality of selection, and in general by the great clarity of all those studies I have read. Perhaps a few of the sections are, relatively to some others, of rather light weight. But it would be unfair, in a necessarily brief notice, to choose any contribution for special blame or praise, in a volume which is of very high quality, which will be a part of the necessary furniture of every active centre of psychological experiment, and which is likely to remain, and to hold for many years, a foremost position as a reliable and comprehensive book of reference.

F. C. BARTLETT

A NEW ATLAS

The Oxford Atlas, *edited by Sir Clinton Lewis and J. D. Campbell. Pp. 96 + xxvi + 88. Oxford University Press, London. 1951. 36s. net.*

The integration of the various surveys of different areas of the earth's surface into maps of a scale and projection suitable for an atlas is a formidable task. While incorporating a considerable amount of detail, the compilers of 'The Oxford Atlas' have been able to produce very attractive maps. Most countries are drawn on scales between 1 : 1,000,000 and 1 : 18,000,000: in choosing areas for illustration on the larger scales the needs of British users have been especially considered. Relief is shown by a pleasing and easily distinguishable series of layer tints.

In addition to these topographical maps, seventeen maps illustrate the distribution of climate, vegetation, population, and land use and structure, in selected areas. The structural maps are completely new productions and 'attempt to classify areas by the geological structure most closely related to their relief, namely, their prevailing structure.' This classification is inevitably successful on the smaller-scale maps but leads to awkward and, in some instances, unreal divisions on the more detailed map of Great Britain. A simplified geological map, superimposed with tectonic and geomorphological data, would be more useful.

The atlas is well bound and contains a complete index-gazetteer. Unfortunately the whole production is marred by a large number of errors. A thorough revision will be necessary before another edition is issued.

E. J. ZUCKERMAN

A TREATISE ON ZOOLOGY

Traité de Zoologie: Anatomie, Systématique, Biologie. *Vol. X, Sections I and II. Pp. 1948. Masson et Cie, Paris. 1951. 3600 fr. each.*

With the publication of the two sections of Volume X of the Traité de Zoologie, dealing with all the higher orders of insects with the exception of the coleoptera, which were already covered under Volume IX, it is possible to form some judgment of the value of this impressive summary of our present knowledge of the insects of the world. What is required of such a work? A broad display of the whole pageantry of insect life; a clear statement of the comparative morphology of the diverse types of insects; and a review of what is peculiar in the physiology and ecology of each group. The field is so vast that even the two thousand pages of this volume can reproduce only the main outlines, and a prime need is a guide to the literature where further details are to be found.

On the whole, these requirements have been admirably met. The range of insect life is certainly magnificently displayed. The copious illustrations in black and white are almost uniformly excellent: many of them are original, and all the drawings have been re-drawn so that all are in one style. The whole is enlivened with a few half-tone reproductions of photographs and a few coloured plates. Each order or sub-order is treated by a different author, who is often a well-known authority in his group. E. Séguy on the flies, E. Pruvot on the hymenoptera, P. Pesson on the homoptera, L. Berland and J. Bernard on the hemiptera. There are naturally some individual differences in the treatment in the sections on flies or hymenoptera about equal numbers of pages are devoted to generalities and systematics, whereas the systematics of lepidoptera occupy little more than a quarter of the 270 pages given to this order. The section on the homoptera is a highly scientific account of a difficult sub-order; that on the lepidoptera by J. Bergeyne, apart from the admirable treatment of the reproductive system, is rather more popular in character. As a guide to the literature some sections are good, but others

abound in generalizations with no indication of their source. This criticism applies particularly to those parts dealing with physiology, but these can be properly judged only when Volume VIII, on insect physiology and ecology in general, appears in 1953.

V. B. WIGGLESWORTH

PRACTICAL HYDRAULICS

Compléments d'hydraulique, *deuxième partie, by L. Escande. Pp.* 248, *with diagrams and photographs. Dunod, Paris.* 1951. 1900*fr. net.*

This second part, like the first (which was published by Privat of Toulouse in 1947) is a collection of papers and studies of practical interest, most of which have been previously published, with less detail, as communications to the *Académie des Sciences* or contributions to discussions of the *Société Hydrotechnique de France.*

The present volume should be of particular appeal to hydraulic engineers concerned with hydroelectric installations, as all the studies are of practical interest.

In one paper the author treats extensively of certain aspects of water-hammer effects in loaded pipes, with all their possible consequences. This study was made for the Genissiat dam, for which also the author considered by a graphical method the closing of a butterfly valve under heavy load. Another paper on the oscillations in an equilibrium chamber is a development of the well-known Bergeron graphical method. An important chapter deals with problems connected with sector gates over weirs. These problems have been studied both on small-scale models and on the prototype.

The only criticisms one may make are that though there is an outward improvement in presentation, in that this second part is bound, the paper is very poor and quite unsuitable for photographic reproduction; and that the typewritten-style text gives an unfinished aspect to an otherwise admirable and useful book.

A. GORDON-FOSTER

METALLIC CREEP

Creep of Metals, *by L. Rotherham. Pp.* 80 + *i. The Institute of Physics, London.* 1951. 15*s. net.*

This is essentially a physicist's introduction to creep, avoiding technicalities of the design of creep tests, and giving no catalogues of the creep properties of particular metals. The experimental results quoted are all used to illustrate physical principles, and references are skilfully selected from the large and sometimes tedious literature of creep.

The scientific study of creep has progressed from two different standpoints —the analytical, typified by Andrade's resolution of the early stages of creep into β and K components, and the synthetic, typified by Mott and Nabarro's detailed consideration of one particular mechanism of deformation. Research at present is much concerned with finding the connection between the components obtained by analysis of the complete elongation-time curve and those available for its synthesis. Mr Rotherham develops the two approaches side by side, illustrating the connection between them as well as is yet possible. The only serious fault of his presentation is a certain lack of clarity. Thus the account of the theoretical yield strength on p. 21 would not convey to the beginner the distinction between Frenkel's estimate of the strength of a large perfect crystal and Bragg's estimate of the strength of a small crystal, while the account of Orowan's hardening theory of transient creep introduces on p. 40 an idea from the exhaustion theory.

Despite some minor blemishes, this can be commended as an introduction to the physics of metallic creep sufficiently thorough to form an introduction for the specialist, and sufficiently attractive in presentation to make borderline reading for the general physicist and metallurgist.

F. R. N. NABARRO

INSECTICIDES

Chemical Control of Insects, *by T. F. West, J. Eliot Hardy, and J. H. Ford. Pp. xi* + 211. *Chapman and Hall Limited, London.* 1951. 15*s. net.*

The control of harmful insects by chemical means has developed enormously during the eighty years or so that have elapsed since Paris green was first used, with success, to kill the Colorado beetle on potatoes. The pace of development has become progressively accelerated as more synthetic organic insecticides have been discovered, until it is now almost impossible to keep abreast of the newest advances. This little book appears to have been written, for the most part, by about 1947, and many of the latest chemical insecticides are not mentioned; but it will serve as a most useful introduction and guide to the well-established substances, and may be strongly recommended for this purpose. There are not many books available to meet this need. This one is packed with accurate information, though much of it is written in somewhat careless English. The authors recognize that there are other methods of limiting the numbers of insect pests, but these get little sympathy: 'In general,' they write, 'cultural methods are, at the best, palliatives.'

V. B. WIGGLESWORTH

A BRITISH IRONSTONE FIELD

The Northampton Sand Ironstone: Stratigraphy, Structure, and Reserves, *by S. E. Hollingworth and J. H. Taylor. Mem. Geological Survey of Great Britain. Her Majesty's Stationery Office, London.* 1951. 17*s.* 6*d. net.*

The ironstone field dealt with in this memoir now yields more than half the British output of iron ore. Although about 250 million tons of ore have been extracted from it in the past century, the reserves are sufficient to last another 175 years at the present rate of production of 7 million tons a year. The subject is therefore of first-class economic importance. The two authors, now both professors of geology at London University, have done full justice to both the practical and the scientific aspects of the matter. The memoir is a model of organization and concise, clear exposition on all problems connected with the quarrying and preparation of bedded ironstone. There are chapters on stratigraphy, structure, methods of prospecting and sampling, methods of working, and ore preparation, followed by a detailed treatment of the field in five chapters, district by district, to which five other members of the Geological Survey ironstone unit have contributed. In an appendix, the authors give definitions of terms used by them to describe superficial structures due to differential erosion. The petrology of the ironstone was dealt with in a separate memoir published in 1949.

W. J. ARKELL

COMMON SENSE OF SCIENCE

The Common Sense of Science, *by J. Bronowski. Pp.* 154. *Heinemann, London.* 1951. 8*s.* 6*d. net.*

There are not very many books about science readable with profit by scientist and layman alike, but this may justly claim to be one. It is written with infectious enthusiasm from beginning to end. Admittedly, the value

of what Dr Bronowski writes varies considerably from chapter to chapter. We are interested, but not very much impressed, when he is trying to persuade us that artists and scientists are really very much alike after all; or apportioning the blame for the horrors of modern war; or taking us on a headlong rush through the history of science, in the course of which Ray and Linnaeus act as shorthand symbols for the systematic biologists of the past, and Darwin and his grandfather play the same part for the theorists of evolution; or particularly when he is telling us that science is only a means of making a set of reasonable guesses about the future, so that we may take the appropriate action. Palaeontology is itself sufficient to contradict this, because it was mainly built up by men who believed that the past is intrinsically interesting and therefore worth study for its own sake. But the author has not swallowed the whole of the dialectical materialist outlook on science by any means, and when he is concerned with the new ideas of indeterminacy and the effect they are likely to have on scientific and philosophical thought, what he writes is both interesting and valuable: his statement of a difficult subject is particularly clear and helpful.

JOHN R. BAKER

### HETEROCYCLIC COMPOUNDS

Heterocyclic Compounds. Volume 2. Polycyclic Five- and Six-membered Compounds Containing One O or S Atom, *edited by Robert C. Elderfield. Pp. vii + 571. John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1951. 120*s. net.*

The second volume of Elderfield's *Heterocyclic Compounds* contains fourteen chapters: 1, benzofuran and its derivatives (Elderfield and Meyer); 2, isobenzofuran, phthalan, and phthalide (Elderfield); 3, dibenzofuran (diphenylene oxide) (Parham); 4, thionaphthene (Fukushima); 5, dibenzothiophene (Fukushima); 6, coumarins (Wawzonek); *iso*coumarins (Wawzonek); 8, chromones, flavones, and *iso*flavones (Wawzonek); 9, chromenols, chromenes, and benzopyrylium salts: the anthocyanins (Wawzonek); 10, chromanones, flavanones, chromanols, and flavanols: catechin, brazilin, and haematoxylin (Wawzonek); 11, chromans (Wawzonek); 12, xanthones, xanthenes, xanthydrols, and xanthylium salts (Wawzonek); 13, fluorans, fluoresceins, and rhodamines (Wawzonek); 14, thiochromans, and related compounds (Tarbell). Chapters 6–11 on the six-membered heterocyclic compounds will doubtless attract the most attention, as they cover a great number of natural products on which much work is still being done.

The aim of these volumes is to give a general survey of heterocyclic chemistry, with primary emphasis on the principles involved. The present volume, however, lays almost the whole emphasis upon methods of preparation and reactions, which are dealt with in detail and with copious references to the original literature; it would have been of advantage to have indicated which methods are the most important.

It is inevitable that a reviewer should find himself most critical where he has first-hand knowledge, and most researchers will wish to consult the original papers. Few errors have been detected, and the structural formulae are mainly well set out, but many might have been simplified with advantage by the use of the abbreviations Me, Et, and Ph. In spite of these minor criticisms, this book is assured of a general welcome from research workers.

W. BAKER

### HISTORY OF NATURE

The History of Nature, *by C. F. von Weizsäcker. Pp.* 180. *Routledge and Kegan Paul Limited, London.* 1951. 12*s.* 6*d. net.*

The author of this book has become well known in astronomical circles in recent years by his theory of the origin of the solar system, in which the important part played by turbulence and viscous forces is emphasized, and by the application of similar basic ideas to the wider problem of the evolution of the stars.

Here he is concerned with a much broader theme, the history of nature. The book is written from the point of view of the interdependence of natural science and humanistic disciplines. Nature is older than man, who is subject to her laws; so humanistic disciplines presuppose natural science. On the other hand, natural science is made by man for man, and so presupposes the humanistic disciplines. Life can be looked on from two opposing points of view, from that of man and from that of natural science.

After tracing past events in the history of the Earth, the spatial and time structures of the universe are considered. The author is in favour of a universe that is finite both in space and in time. He considers that the doctrine of the infinity of time involves the abandonment of the essentially historic thinking of Christianity. The formation of star systems is discussed; there appears to be an evolution from disorder to order, from chaos to form; then in turn the formation of individual stars, and the formation and evolution of the Earth are considered.

Thus the author comes to the question of the origin of life. It is emphasized that being is older than knowledge, but only knowledge knows what being is. The mysteries of life and of consciousness give rise to philosophical questions: What quality distinguishes man from other living beings? What is the soul? The outer history and the inner history of man are discussed, and the question is posed whether science can carry us beyond pure knowledge into the field of ethics.

This stimulating book, which will well repay reading and re-reading, ends with the quotation from Angelus Silesius:

> Friend, let this be enough. If thou wouldst go on reading,
> Go and thyself become the writing and the meaning.

H. SPENCER JONES

### ORGANIC PREPARATIONS

Preparation of Organic Intermediates, *by D. A. Shirley. Pp. x + 328. John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1951. 48*s. net.*

This book will be compared with the second volume of L. Vanino's *Präparative Chemie*. It contains 450 organic preparations, some of them involving isolation of intermediates, taken, with two exceptions, directly from the literature. The compounds chosen have each satisfied the following criteria: (1) the compound is either not available commercially or, if available, is relatively expensive; (2) its preparation has not been published in 'Organic Syntheses'; (3) either it has a simple structure and contains functional groups which make it useful as an intermediate, or its preparation involves a generally useful type of reaction. It is stated of each starting material that either it is available commercially at relatively low cost, or its preparation is described in 'Organic Syntheses' or in the present volume itself.

It might have been expected that the preparations would be taken largely from the less available journals, but this is not so. The distribution is as

follows: Journal of the American Chemical Society, 50 per cent.; *Berichte*, 15 per cent.; Journal of the Chemical Society, 10 per cent.; Journal of Organic Chemistry, 5 per cent.; *Annalen der Chemie*, 5 per cent.; *Bulletin de la Société Chimique*, 3 per cent.; *Helvetica Chimica Acta*, 2 per cent.; twelve other journals, 10 per cent.

This will prove a useful book to those who are not in a position to consult the original literature, but the chances of finding a desired preparation in it are not high. The type, equations, and graphic formulae are excellent; besides a general index there are indexes of molecular formulae and types of reaction. The only error noticed is in the table of contents on page vii.

W. BAKER

### A PALAEOGEOGRAPHICAL ATLAS

A Palaeogeographical Atlas of the British Isles and Adjacent Parts of Europe, *by L. J. Wills. Blackie and Son Limited, London and Glasgow.* 1951. 21*s. net.*

The historical geologist relates variations in the nature of sedimentary rocks and the fossils they contain to their conditions of deposition, and interprets them in terms of the changing distribution of land and sea. In this, he synthesizes the specialized work of the sedimentary petrologist, the palaeontologist, and the structural geologist; but the help they can give is limited by the inadequate exposures which provide their samples. Thus one may be confronted with little more than the upturned edge of a sheet of rock, the edge itself largely obscured by soil and vegetation, from which to deduce the lateral variation of that sheet in thickness, lithology, and faunal content, and its relation to underlying formations. Naturally, the palaeogeographic conclusions are often far from precise and are always provisional, although, in areas where economic possibilities provide the funds for drilling, they may at any time have to stand rigorous testing.

Britain is fortunate in having representatives of all the geological systems, but, for a variety of reasons, some are far better known than others. Professor Wills is to be congratulated as much on his courage as on his performance in presenting in map form a complete series of palaeogeographic restorations from Lower Palaeozoic to Pleistocene. Each of the twenty-two plates summarizes a wealth of detail, sifted and interpreted by a general stratigrapher whose judgment and experience are universally acknowledged. It is probable that, even so, the specialist in every system will find points of disagreement, but Wills disarms criticism with the remark that success in knocking down his Aunt Sally carries with it the obligation to set up a better. Teachers, who have every reason to be grateful to the author, have a corresponding obligation to make clear to their pupils exactly what this atlas purports to be. A special word of appreciation is due to the publishers for their admirable production.

O. M. B. BULMAN

### INSECTS AS HUMAN FOOD

Insects as Human Food: A Chapter of the Ecology of Man, *by F. S. Bodenheimer. Pp.* 1–352. *Dr W. Junk, The Hague.* 1951. *fl.*10 *net.*

One of the most interesting features of this book is the evidence it provides that insects may be important sources of proteins, fats, vitamins, and minerals, and thus may be valuable foods in countries—especially tropical countries—in which the available diets are mainly vegetarian. In some of these countries, life may be dominated by the perpetual search for food, and many animals, from crocodiles to snails, are eaten; but insects, whether they be locusts, white or other ants, caterpillars, water-boatmen, or any of the other species discussed in this book, may also be important sources of essential dietary elements.

The analyses of various kinds of insects quoted by Bodenheimer show that they can provide astonishing quantities of proteins, fats, vitamins, salts, and minerals. Thus one analysis of white ants (termites) shows a content of 44·4 per cent. fat and 36 per cent. protein; 100 g of them provide 561 calories, so that they are among the richest foods and superior to some other animal foods. They are also rich in phosphates and potash, and they yield a colourless oil useful for frying. A clear, fairly hard soap can be made from termite oil. The other analyses quoted by Bodenheimer—of caterpillars, silkworm pupae, locusts, and other insects—show that those species which are eaten in large quantities are also valuable as food. As a source of energy and pleasure, the honey of bees has been collected since Palaeolithic times, and Bodenheimer has gathered together a great deal of information about its use by various peoples, and about their methods of collecting and storing it.

One can, indeed, find both profitable and entertaining reading in every chapter of this book, for it discusses not only the various insects eaten in Australia, Africa, Asia, and the Americas, but the history of insect-eating up to the present day. Man's first interest in insects was, the author thinks, aroused by their possible food-value, and, although they are not nowadays eaten in Europe, that is the result of custom and prejudice rather than of aversion to them.

The 47 illustrations add to the value of the book and there is a good bibliography, which collects the scattered and extensive literature. There is, unfortunately, no index; this is a serious omission in a book providing so much detailed information.

G. LAPAGE

### INDUSTRIAL CHEMISTRY

Traité de Chimie Industrielle, *by Paul Baud. Three volumes, totalling* 3072 *pages. Masson et Cie, Paris.* 1951. 15,400 *fr.* (*unbound*); 17,600 *fr.* (*bound*).

The appearance of a fourth edition of this work, the first since 1943, is a sufficient indication of its established position in chemical literature. It is designed primarily for advanced students in universities and technical schools, but it is a valuable work of reference for all those interested in industrial chemical processes. The three volumes—which may be purchased separately — deal respectively with heavy chemicals, derivatives of metals and metalloids, and organic chemicals. The text is based on a wide definition of the chemical industry, including, for example, such processes as sugar refining, papermaking, the extraction of essential oils, and the preparation of tannins.

So comprehensive a work cannot, of course, be briefly reviewed except in general terms. It can be said, however, that by sampling a few topics which have grown to be important only during the last few years, such as the manufacture of silicones, the publishers' claim that the previous edition has been thoroughly revised is found to be amply substantiated. The author has put chemists in his debt by undertaking the heavy task of keeping this well-tried work thoroughly up to date, particularly at a time when the importance of technological studies is being increasingly widely recognized.

# Some books received

(*Note.* Mention of a book on this page does not preclude subsequent review.)

BIOLOGY

Carbon Dioxide Fixation and Photosynthesis. *Symposia of the Society for Experimental Biology, No. 5. Pp.* 342, *with various half-tone and line diagrams. Cambridge University Press, London* 1951. 42*s. net.*

Soviet Genetics, *by Alan G. Morton. Pp.* 174. *Lawrence and Wishart, London.* 1951. 15*s. net.*

BOTANY

Trace Elements in Plant Physiology. *A Symposium arranged by the International Union of Biological Sciences. Pp.* 141, *with half-tone and line illustrations. Chronica Botanica Company, Waltham, Mass.; Wm. Dawson and Sons Limited, London.* 1951. $4.50 *net.*

CHEMISTRY

German Books on Chemical and Cognate Subjects published 1939–50. *Second revised and extended edition by A. E. Cummins and S. Vince. Pp.* 102. *Lange, Maxwell, and Springer Limited, London.* 1951. *Supplied free of charge on request.*

Natural and Synthetic High Polymers, *by K. H. Meyer. Pp.* 891, *with line and half-tone illustrations. Interscience Publishers Inc., New York.* 1951. $15 *net.*

Organic Syntheses (Vol. 31), *by R. S. Schreiber. Pp.* 122. *John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1951. 22*s. net.*

Radioactivity Applied to Chemistry. *Edited by Arthur C. Wahl and Norman A. Bonner. Pp.* 604. *John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1951. 60*s. net.*

Réarrangements Moléculaires et Inversion de Walden. *Colloque tenu à Montpellier 24th–29th April,* 1950. *Pp.* 152. *Centre National de la Recherche Scientifique, Paris.* 1951. 44*s. net.*

Statistical Methods for Chemists, *by W. J. Youden. Pp.* 126. *John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1951. 24*s. net.*

ENGINEERING

Dizionario d'Ingegneria, *edited by Eligio Perucca. Vol. I, A–CER. Pp.* 1052, *with* 2200 *line drawings in the text. Unione Tipografico Editrice Torinese, Turin.* 1951. 12,000 *lire.*

GENERAL SCIENCE

Bibliography of Scientific and Technical Dictionaries, *by J. E. Holmstrom. Pp.* 227. *UNESCO, Paris.* 1951. 4*s. net.*

Inter-Commonwealth Postgraduate Scholarships in Science. *Issued by the British Commonwealth of Nations' Scientific Liaison Offices. Pp.* 82. *Her Majesty's Stationery Office, London.* 1951. 5*s. net.*

International Conference on Science Abstracting—Final Report. *Pp.* 192. *UNESCO, Paris.* 1951. 12*s* 3*d. net.*

Laboratory Instruments: their Design and Application, *by A. Elliott and J. Home Dickson. Pp.* 414, *with various line diagrams. Chapman and Hall Limited, London.* 1951. 32*s. net.*

INDUSTRY

The Chemical Technology of Dyeing and Printing (Vol. II), *by Louis Diserens. Translated and revised from the second German edition by Paul Wengraf and Hermann P. Baumann. Pp.* 446. *Reinhold Publishing Corporation, New York; Chapman and Hall Limited, London.* 1951. 96*s. net.*

Plastics Progress. *Papers and discussion at the British Plastics Convention,* 1951. *Edited by Phillip Morgan. Pp.* 310. *Published for* British Plastics *by Iliffe and Sons Limited, London.* 1951. 50*s. net.*

Seaweed Utilization, *by Lily Newton. Pp.* 188, *with numerous half-tone and line illustrations. Sampson Low, Marston, and Company Limited, London.* 1951. 21*s. net.*

MATHEMATICS

Advanced Five-figure Mathematical Tables, *by C. Attwood. Pp.* 69. *Macmillan and Company Limited, London.* 1951. 4*s.* 6*d. net.*

MEDICINE

Documenta Ophthalmologica, *Vols. V–VI. Pp.* 585, *with various line and half-tone diagrams. Dr. W. Junk, Publisher, The Hague.* 1951. *fl.* 72 *net.*

Mental Prodigies, *by Fred Barlow. Pp.* 256. *Hutchinson's Scientific and Technical Publications, London.* 1951. 12*s.* 6*d. net.*

PHARMACY

Insect Control by Chemicals, *by A. W. A. Brown. Pp.* 817, *with several half-tone and line illustrations. John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1951. 100*s. net.*

Mécanisme de la Narcose. *Colloques Internationaux du Centre National de la Recherche Scientifique. Pp.* 215. *C.N.R.S., Paris.* 1951. 35*s. net.*

Pharmacopoea Internationalis, *Vol. I. Pp. xviii* + 406. *World Health Organization, Geneva.* 1951. 35*s. net.*

PHYSICS

The Conductivity of Electricity through Gases, *by K. G. Emeléus. Pp.* 99, *with* 37 *diagrams. Methuen and Company Limited, London.* 1951. 5*s.* 6*d. net.*

The Electric Current, *by P. Dunsheath. Pp.* 211, *with many half-tone and line illustrations. G. Bell and Sons Limited, London.* 1951. 18*s.* 6*d. net.*

Electrical Phenomena at Interfaces, *edited by J. A. V. Butler. Pp.* 309, *with several line diagrams. Methuen and Company Limited, London.* 1951. 32*s.* 6*d. net.*

Elementary Particles, *by Enrico Fermi. Pp.* 110. *Oxford University Press, London.* 1951. 12*s.* 6*d. net.*

Experimental Spectroscopy, *by R. A. Sawyer (second edition). Pp.* 358, *with several half-tone and line illustrations. Chapman and Hall Limited, London.* 1951. 30*s. net.*

Industrial High Vacuum, *by J. R. Davy. Pp.* 243, *with several line diagrams. Sir Isaac Pitman and Sons Limited, London.* 1951. 25*s. net.*

Photoelectric Tubes, *by A. Sommer. Pp.* 118, *with several line drawings. Methuen and Company Limited, London.* 1951. 8*s.* 6*d. net.*

Radiation Monitoring in Atomic Defence, *by Dwight E. Gray and John H. Martens. Pp.* 122, *with line and half-tone illustrations. Macmillan and Company Limited, London.* 1951. 15*s. net.*

Theory of Electrons, *by L. Rosenfeld. Pp.* 119. *North-Holland Publishing Company, Amsterdam.* 1951. *fl.* 17.50 *net.*

Thermodynamics of Irreversible Processes, *by S. R. de Groot. Pp.* 242. *North-Holland Publishing Company, Amsterdam.* 1951. *fl.* 17.50 *net.*

Typical Microstructures of Cast Iron. *Pp.* 54, *with* 41 *illustrations. British Cast Iron Research Association, Birmingham.* 1951. 15*s. to members of the Association;* 21*s. to non-members.*

Vacuum Physics. *A symposium held by the Midland Branch of the Institute of Physics in Birmingham on 27th and 28th June,* 1950. *Pp.* 80, *with various line and half-tone illustrations. The Institute of Physics, London.* 1951. 15*s. net.*

*Corrigendum.* The name Tarlington, on page 223 of our October 1951 issue, should have been Turlington.

# Notes on contributors

W. J. ARROL,
*B.Sc., Ph.D.,*

Was born in 1915, and is a graduate of London University. His interest in the chemical side of radioactive work dates from 1935. From 1940 to 1943 he served in the R.N.V.R. as a radar officer, and in 1943 joined the Canadian atomic energy project at Montreal. In 1945, he returned to England and spent the next three years lecturing in chemistry at London University. He joined the atomic energy research establishment at Harwell in 1948, and became senior chemist in the newly formed isotopes division, where he still is.

ANDRÉ LWOFF,
*M.D., D.Sc.,*

Was born in 1902. Studied at the University of Paris in the faculties of medicine and science. His scientific career has been at the *Institut Pasteur*, where he is now head of the department of microbial physiology. He was a Rockefeller Foundation fellow at the *Kaiser-Wilhelm Institut*, Heidelberg, in 1933, and at the Molteno Institute, Cambridge, in 1936. He was Dunham lecturer at Harvard University in 1948.

His researches have been on the evolutionary cycle and the morphogenesis of ciliates, on the nutrition of protozoa, on bacterial growth-factors and their physiological role, and on lysogenic bacteria. His books include *L'Évolution Biochimique* (Paris, 1944); 'Problems of Morphogenesis in Ciliates' (New York, 1950), and 'Biochemistry of Protozoa' (New York, 1951).

JOHN HANCOCK,
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Is a graduate (1935) of the University of Helsinki. He has been employed in practical, administrative, and research activities in agriculture in Finland, Australia, New Zealand, and the South Sea Islands, and is now chief animal geneticist at the Ruakura animal research station, Department of Agriculture, Hamilton, New Zealand. His interests lie in animal breeding and behaviour.

E. BOYLAND,
*Ph.D., D.Sc.,*

Is professor of biochemistry in the University of London at the Chester Beatty research institute of the Royal Cancer Hospital, where he has worked (except for the war years) since 1931. In addition to work on carcinogenesis and the metabolism of hydrocarbons, he has worked with colleagues on the chemotherapy of cancer, and on the nature of the carbohydrate metabolism of tumours. During the war, he investigated biochemical and pharmacological problems of chemical warfare for the Ministry of Supply, and diseases of animals for the Ministry of Agriculture. Before starting work on cancer research, he studied the biochemistry of muscle in the physiological laboratory of the University of Manchester and at the *Kaiser-Wilhelm Institut*, Heidelberg, with Otto Meyerhof. As Grocers' Company scholar and later Beit Memorial fellow at the Lister Institute for Preventive Medicine, London, he carried out researches with the late Sir Arthur Harden on the biochemistry of yeast. In 1948 he received the Judd award for cancer research in New York.

L. R. G. TRELOAR,
*B.Sc., Ph.D., D.Sc., F.Inst.P.,*

Was born in 1906. He studied physics at Reading University under J. A. Crowther. From 1929 to 1938 he was engaged in research on radio valve developments at the research laboratories of the General Electric Company. He joined the newly formed British Rubber Producers' Research Association in 1938, working first with E. K. Rideal and J. K. Roberts at the colloid science laboratory, Cambridge, and later with G. Gee at the Association's Welwyn Garden City laboratories. He has published numerous experimental and theoretical papers on rubber physics, and is author of 'The Physics of Rubber Elasticity (Clarendon Press, 1949).

Since 1949 he has been senior physicist to the British Rayon Research Association, and has been working at the Davy Faraday laboratory of the Royal Institution on the physical properties of textile fibres.

C. W. WARDLAW,
*Ph.D., D.Sc., F.R.S.E.,*

Was born in 1901, and was a student and member of staff in the botany department, Glasgow University, from 1918 to 1928. His earlier interests were in plant morphology and pathology, and in mycology. In 1928 he joined the staff of the Imperial College of Tropical Agriculture, Trinidad, B.W.I., to investigate problems relating to diseases of the banana and the transport of tropical fruit. Since 1940, he has been professor of cryptogamic botany in the University of Manchester. While still retaining an active interest in the problems of mycology and plant pathology, his personal research during the past ten years has been on morphogenesis in plants, especially by the use of experimental methods.

SIRO TAVIANI

Was born at Vinci in 1889 and studied medicine at the University of Florence. He was director of the clinic of dental medicine in the University of Perugia from 1930 to 1942, and is a member of numerous Italian and other academies and learned societies. He has published more than a hundred articles (for the most part original) on various stomatological subjects, particularly in the field of dental morphology, and has put forward a new hypothesis concerning the morphological origin of human teeth and of mammalian teeth in general. He has also made many historical researches on Leonardo da Vinci. At present, he is director of the biological research laboratory in the *Scuola Perfezionamento, Clinica Odontoiatrica*, University of Rome.

# ENDEAVOUR

The British quarterly scientific review ENDEAVOUR was first published in January 1942. Its purpose was to enable men of science, and particularly British men of science, to speak to the world in an hour when not only nations but the internationalism of science suffered the dangers of warfare. For the better fulfilment of this purpose ENDEAVOUR was from the first published in four separate editions—English, French, Spanish, and German. An Italian edition has been published since January 1948. Today the situation is happily different, but there can be no lasting peace without full and sincere co-operation between nations in every realm of human enterprise. In the scientific field ENDEAVOUR can thus play as useful a part in peace as it did in war, and for this reason the decision has been taken to make its publication permanent.

ENDEAVOUR is distributed without charge to senior scientists, scientific institutions, and libraries throughout the world, the guiding principle being that of helping scientists overseas to maintain those contacts which their British colleagues have always so much valued. Within these limits the Editors are at all times glad to consider the addition of new names to the mailing list.

*Made and printed in Great Britain at* THE KYNOCH PRESS, *Witton, Birmingham, 6, for the publishers,*
IMPERIAL CHEMICAL INDUSTRIES LIMITED, *London, S.W.1*